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THE CAUSE AND THE CONTROL OF DYSPNEA IN DISEASE OF THE LUNGS. By GEORGE WILLIAM NORRIS, A.B., M.D. 157

FURTHER OBSERVATIONS ON THE NATURE AND TREATMENT OF CHRONIC NEPHROSIS. By ALBERT A. EPSTEIN, M.D. 167

THE PREVALENCE OF FREE HYDROCHLORIC ACID IN CASES OF CARCINOMA OF THE STOMACH. By HOWARD R. HARTMAN, M.D. 186

THE RELATION OF ACROMEGALY TO THYROID DISEASE: WITH A STATISTICAL STUDY. By J. M. ANDERS, M.D., LL.D., and H. L. JAMESON, M.D. 190

EPILEPTOID OR FAINTING ATTACKS IN HYPOPITUITISM. By L. PIERCE CLARK, M.D. 211

THE UREA CONCENTRATION TEST. By DONALD R. BLACK, M.D. 218

BILIARY TRACT DISEASE: SOME LESSONS LEARNED FROM DUODENOBILIARY DRAINAGE. FUTURE PROBLEMS. CITATION OF CASES. By B. B. VINCENT LYON, A.B., M.D., HENRY J. BARTLE, B.S., M.D., and RICHARD T. ELLISON, B.S., M.D. . . 223

THE DIAGNOSIS OF PERITONITIS AND PERITONEAL TRANSUDATES IN INFANTS BY MEANS OF ABDOMINAL PUNCTURE WITH THE CAPILLARY TUBE. By B. S. DENZER, M.D. 237

SOME STATISTICS CONCERNING PNEUMONIA AND EMPYEMA IN CHILDREN. By ELIZABETH GLENN-RAVDIN, M.D. 246

UNKNOWN FORMS OF ARTERITIS, WITH SPECIAL REFERENCE TO THEIR RELATION TO SYPHILITIC ARTERITIS AND PERIARTERITIS NODOSA. By FRANCIS HARBITZ, M.D. 250

POSTOPERATIVE DIETOTHERAPY. By WARREN T. VAUGHAN, M.D., and NELLIE H. VAN DYKE, B.S. 272

ADDISON'S DISEASE: A CASE OF TUBERCULOSIS OF THE ADRENALS. By ROBERT A. KEILTY, M.D. 282

NOTICE OF GORGAS MEMORIAL INSTITUTE . . . . . ADV. PAGE 28

DE ROALDES PRIZE . . . . . " " 28

INDEX TO ADVERTISERS . . . . . " " 18

Contents continued on page x

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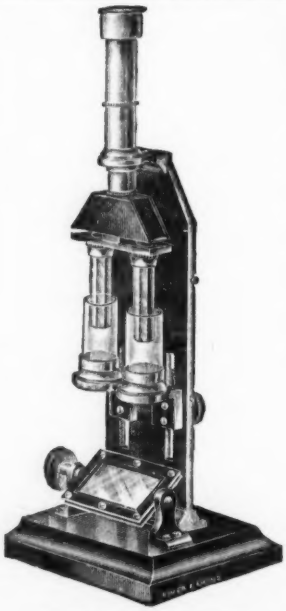

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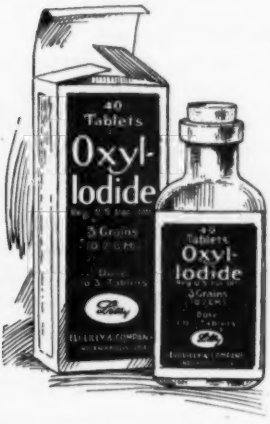

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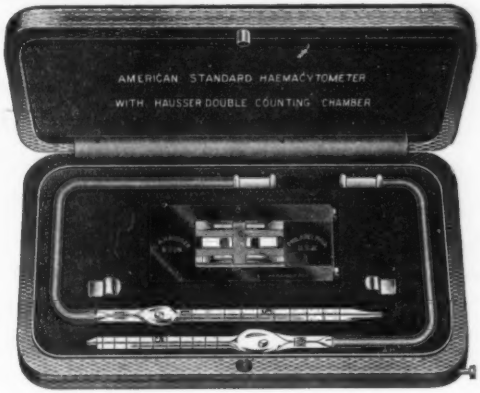

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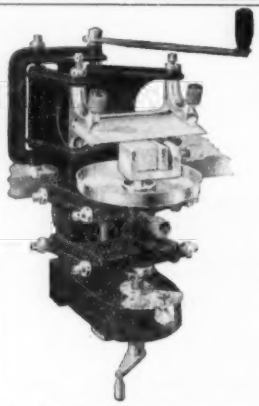

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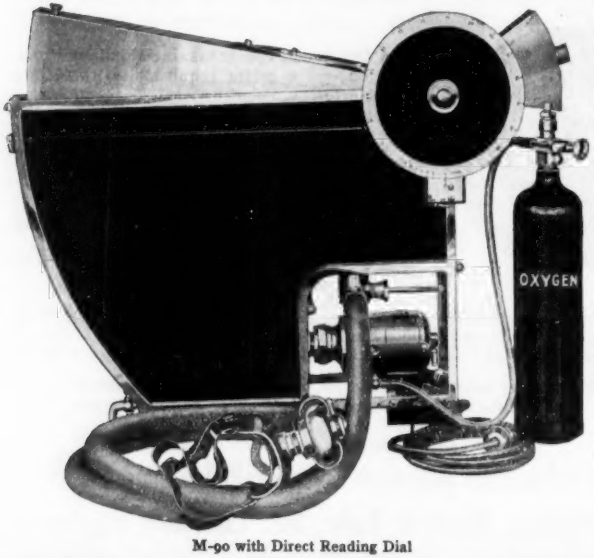

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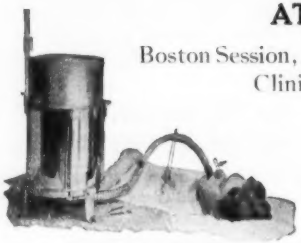

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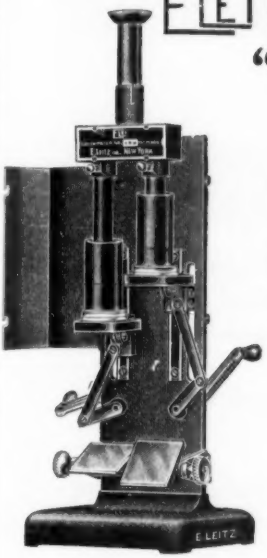

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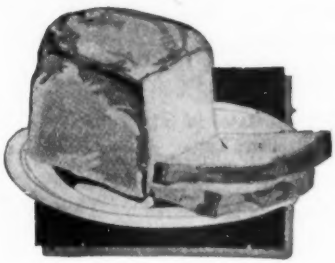

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CONTENTS

ORIGINAL ARTICLES

The Cause and the Control of Dyspnea in Disease of the Lungs 157
By George William Norris, A.B., M.D., Philadelphia.

Further Observations on the Nature and Treatment of Chronic Nephrosis 167
By Albert A. Epstein, M.D., New York.

The Prevalence of Free Hydrochloric Acid in Cases of Carcinoma of the Stomach 186
By Howard R. Hartman, M.D., Rochester, Minn.

The Relation of Acromegaly to Thyroid Disease: with a Statistical Study 190
By J. M. Anders, M.D., LL.D., and H. L. Jameson, M.D., Philadelphia.

Epileptoid or Fainting Attacks in Hypopituitism 211
By L. Pierce Clark, M.D., New York City.

The Urea Concentration Test 218
By Donald R. Black, M.D., Kansas City, Mo.

Biliary Tract Disease: Some Lessons Learned from Duodenobiliary Drainage. Future Problems. Citation of Cases 223
By B. B. Vincent Lyon, A.B., M.D., Henry J. Bartle, B.S., M.D., and Richard T. Ellison, B.S., M.D., Philadelphia, Pa.

The Diagnosis of Peritonitis and Peritoneal Transudates in Infants by Means of Abdominal Puncture with the Capillary Tube . . . 237
By B. S. Denzer, M.D., New York.

Some Statistics Concerning Pneumonia and Empyema in Children . . 246
By Elizabeth Glenn-Ravdin, M.D., Philadelphia.

(*Contents continued on page 12*)

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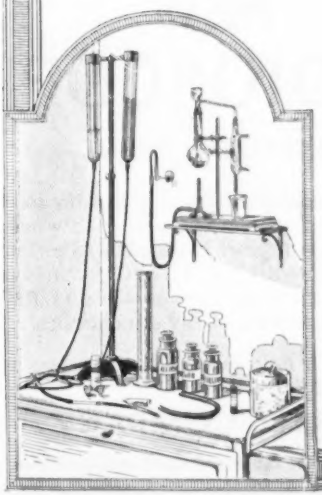

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CONTENTS—(*Continued*)

Unknown Forms of Arteritis, with Special Reference to their Relation to Syphilitic Arteritis and Periarteritis Nodosa 250
By Francis Harbitz, M.D., Christiania, Norway.

Postoperative Dietotherapy 272
By Warren T. Vaughan, M.D., and Nellie H. VanDyke, B.S., Richmond, Va.

Addison's Disease: A Case of Tuberculosis of the Adrenals 282
By Robert A. Keilty, M.D., Danville, Pa.

REVIEWS

X-Rays and Radium in the Treatment of Diseases of the Skin. By George Miller MacKee, M.D. 290
Traumatic Surgery. By John J. Moorhead, M.D. 291
Prosthetic Dentistry. By Douglas Gabell, L.R., C.P., M.R.C.S., L.D.L. 292

PROGRESS OF MEDICAL SCIENCE

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UNDER THE CHARGE OF
W. S. THAYER, M.D., ROGER S. MORRIS, M.D.,
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Acute Circumscribed Edema (Quincke) 293
Herpes Zoster Associated with Disease of Internal Organs 294

(*Contents continued on page 14*)

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Flocculation Reactions in Syphilis with Especial Reference to the Meinicke and Sachs-Georgi Reactions 294
Viability of Spirocheta Pallida in Excised Tissue and Autopsy Material . 295
Complement-fixation Tests with Two Antigens 295
Studies in the Standardization of the Wassermann Reaction 295
Salt solution in Increased Intracranial Tension 296
Jejunal Ulcer 296
Studies in Reduction of Bone Density 297

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND ALVIN E. SIEGEL, M.D.

A Contribution to the Topographic Anatomy of the Thymus Gland with Particular Reference to its Changes at Birth and in the Period of the Newborn 298
Calcium and Phosphorus in the Serum in Relation to Rickets 299
The Casein of Cows' Milk and Human Milk in their Relation to Infant Feeding (the Action of Rennin on Casein) 299
Lesions of the Corpus Striatum in Childhood, with a Report of Clinical Cases (Illustrating Various Syndromes) 300
Some Observations on the So-called Inanition Fever of the Newborn . 300
Malnutrition in Children of the Well-to-do 301
Acute Rheumatic Fever and Its Variants in Childhood and Adolescence 302

(*Contents continued on page 16*)

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CONTENTS—(*Continued*)

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.

Treatment of Sterility by the Use of the Intra-uterine Stem Pessary . . 302
Indirect Expulsion of the Placenta 303

GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D., AND FRANK B. BLOCK, M.D.

Drainage in Pelvic Surgery 303
Embolism after Hysterectomy for Myoma 304
Management of Renal Tuberculosis 305

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

OSKAR KLOTZ, M.D., C.M., AND DE WAYNE G. RICHEY, B.S., M.D.

Experimental Rickets in Rats. I. A Diet Producing Rickets in White Rats and its Prevention by the Addition of an Inorganic Salt . . 306

(*Contents continued on page 18*)

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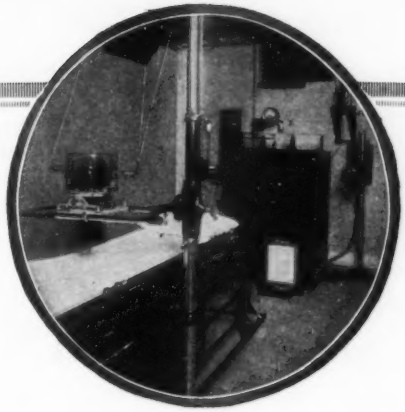

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CONTENTS—(*Continued*)

Note on the Preservation of Stock Strains of Treponema Pallidum and on the Demonstration of Infection in Rabbits 307
Bacteriologic Studies of the Upper Respiratory Passages 307
Relation between the Virulence of Streptococci and Hemolysin . . . 308
Acute Respiratory Infection in Man Following Inoculation with Virulent Bacillus Influenzæ 308
Experimental Studies of the Nasopharyngeal Secretions from Influenza Patients 309
Albumin Reaction in Sputum 310
The Incidence of Bovine Infection in Tuberculous Meningitis 311

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D., AND GEORGE W. McCOY, M.D.

Studies of the Phenomenon of d'Hérelle with Bacillus Dysenteriæ . . . 311
Hypochlorite Process of Oyster Purification 312

INDEX TO ADVERTISERS

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Apparatus and Instruments

(Bacteriological, Diagnostic, Sterilizers, etc.) PAGE

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Wilmot Castle Co. 7
Eimer and Amend . . . 2d Cover
Electro Surgical Instr. Co. 16
E. Leitz, Inc. 9
Palo Co. 12
Physicians' Supply Company of Phila. . . . . 3d Cover
Harvey R. Pierce Co 10
Precision Ther. and Instr. Co. 21
Rieker Instr. Co. 7
Sanborn Co. 8
Spencer Lens Co. 6
Steele Glass Co. . . . . ..
Arthur H. Thomas Co. . . . 3
Toledo Technical Appliance Co. 6
Williams, Brown & Earle 7

Binders, Supporters, etc.

Katherine L. Storm, M.D. 21

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Arlington Chemical Co. . . 15
E. Bilhuber, Inc. 15
Ciba Co. . . . . 4th Cover
Dermatological Research Laboratories. 19
Diarsenol Co., Inc. 23
Fairchild Bros. & Foster . . 5
Hoffmann-LaRoche Chemical Works. 14
Eli Lilly & Co. 1
Maltbie Chemical Co. . . . 21
Merck & Co. 15
H. A. Metz Laboratories. 11
Loeser's Intravenous Solutions 24
Parke, Davis & Co. 27
Riedel & Co. 21
Schering & Glatz, Inc. . . . 19
Sharp & Dohme. 13
Dr. G. H. Sherman. 13
E. R. Squibb & Sons. 20
Upsher Smith, Inc. 7
George J. Wallau. 26
Winthrop Chemical Co. . . 26

Dry Milk

Dry Milk Co. . . . . 3d Cover

Foods, Beverages, etc.

Cellu Flour Mill 25
Farwell & Rhines. 22
The Fleischmann Co. 2
Horlick's Malted Milk Co. 22
Lister Bros., Inc. 9
Mellin's Food Co. . . 4th Cover

Resorts and Hotels

Battle Creek Sanitarium . . 36
Glen Springs. 22
Waldorf-Astoria. 4

Sutures & Ligatures

Davis & Geck, Inc. . . 2d Cover

X-Ray Apparatus, Tubes, etc.

Victor *X*-Ray Corp. 17

Miscellaneous

Colgate & Co. . . . . ..
Kalak Water Co. 36
Lea & Febiger 29-35

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ORIGINAL ARTICLES.

THE CAUSE AND THE CONTROL OF DYSPNEA IN DISEASE OF THE LUNGS.[1]

By George William Norris, A.B., M.D.,

PROFESSOR OF CLINICAL MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA; PHYSICIAN TO THE PENNSYLVANIA HOSPITAL; FELLOW OF THE COLLEGE OF PHYSICIANS OF PHILADELPHIA; COLONEL, M. R. C., U. S. ARMY.

Dyspnea—difficult or labored breathing—occurs if the hydrogen ion content of the blood is raised and the subject is unable to increase his pulmonary ventilation promptly and adequately. With dyspnea one practically always finds hyperpnea, but the reverse does not necessarily follow. Dyspnea implies subjective discomfort. The hydrogen content of the blood may be raised by increase of (*a*) carbon dioxide and (*b*) lactic and other acids of metabolism. The role of anoxemia as a cause of dyspnea is of much less importance. Its effect is an indirect one through its influence upon the sensitivity of the respiratory center.

Pulmonary ventilation is so closely connected with cardiac efficiency that one has to consider this factor, even though one's thesis be limited to dyspnea due to disease of the respiratory organs.

Orthopnea, an exaggerated form of dyspnea in which the subject must sit up in order to get his breath, has been variously explained. It is generally assumed that the erect position is more comfortable because it favors the return of blood from the cerebral vessels and because it enlarges the thoracic cavity and increases the reserve air in the lungs, etc. Recently, however, since the relationship between

[1] Read before the American Climatological and Clinical Association, June, 1921.

anoxemia and shallow breathing has been pointed out,[2] it appears not unlikely that an erect position is chiefly beneficial because it minimizes uneven ventilation of the lungs.

Among the factors which will require special consideration are (1) the dead space; (2) pulmonary ventilation; (3) lung volume.

I. The Dead Space. By this we understand the whole of the respiratory passages into which air is inhaled during respiration excepting the alveoli of the lung—nose, mouth, trachea, bronchi, etc. During shallow breathing the dead space is relatively large; during deep breathing it is small. The dead space varies not only relatively, but actual variation may be brought about by changes in the size of the infundibula (Hoover). It is also interesting to note that the dead space for oxygen is larger than that for carbon dioxide, a difference which is probably due to the fact that considerable quantities of CO_2 may diffuse out of the bloodvessels in the walls of the respiratory channels. However, the dead space is essentially physiological rather than an anatomical conception. "The magnitude of the space depends on the physiological efficiency of the respiratory surface in relation to the supply of venous blood and fresh air" (Haldane).

While there is still no unanimity of opinion on the subject, the normal dead space for resting subjects is generally accepted as lying between 120 and 140 cc. Some investigators found the dead space much larger during deep breathing, though Pearce found but little difference. According to Krogh and Lindhard, maximal pulmonary inflation may increase the dead space by 100 cc.

But the dead space may also be increased by involvement of the pulmonary parenchyma. Thus if the alveoli of one lobe or one lung cease to functionate as a result of pulmonary consolidation or circulatory disturbance an increased dead space results. Again, edema of the lungs or exudate in the bronchi not only increases the dead space but also decreases the pulmonary ventilation. Further, if the dead space is large increase in ventilation may accomplish but little.

II. Pulmonary Ventilation. By pulmonary ventilation one understands the total amount of air which enters and leaves the lungs. If one assumes that the dead space for a given subject is variable, pulmonary ventilation is not synonymous with alveolar ventilation. Pulmonary ventilation is regulated by the medullary respiratory center, which is in turn affected by (*a*) afferent nervous stimuli and chiefly through the vagus and by (*b*) chemical factors.

The respiratory center may vary in its threshold of response. Thus caffein and anoxemia are supposed to increase and opium and certain toxins to decrease its irritability.

Of far greater importance, however, is the hydrogen ion concentra-

[2] Haldane, Meakins and Priestley: Jour. Physiol., 1919, **52**, 433.

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tion of the blood, a very small increase of which produces an immediate response on the part of the respiratory center. Thus any increase in the CO_2 tension of the blood promptly increases the respirations, whereas forced deep breathing, which depletes the blood of CO_2, is followed almost invariably by apnea (acapnia). Other acids in the blood, such as those which occur in the acidosis of diabetes, have a similar stimulating effect.

III. Lung Volume. The term *vital capacity* is applied to the maximum quantity of air which can be forced out of the lungs after a forced maximal inspiration. The air still remaining in the lungs is known as residual air, and these two factors combined constitute the total lung capacity. The air which enters and leaves the lung during quiet breathing is called the tidal air and the pulmonary capacity at the middle of such quiet breathing is known as the midcapacity.

All of the foregoing factors are subject to individual and temporal variation. Thus midcapacity is increased by a change of posture from the recumbent to the erect position. It is also increased by dyspnea, high altitude and exposure to cold.

Exercise may enormously increase pulmonary ventilation, the reserve factor of safety being estimated at 90 per cent as compared to 13 per cent usually accredited to the normal heart. As a rule, pulmonary volume decreases promptly after cessation from exertion, although it may persist for one or two days. Pulmonary volume has been found increased in the players of wind instruments and in glass-blowers (Hewlett).

Pathological pulmonary distention accompanies stenosis of the respiratory passages, and it may be a local phenomena if the bronchus of a given lobe or part of a lobe is constricted.

Asthma usually causes great pulmonary distention. Sometimes this disappears within a few days, but often, especially with recurrent paroxysms, it tends to remain more or less permanently.

Dyspnea and Cyanosis. It may not be amiss at this stage of our discussion to point out certain facts regarding dyspnea and cyanosis. It is well known that a patient may have marked air hunger and yet not be cyanotic, and, on the contrary, he may be quite blue without dyspnea. Thus a patulous cardiac septum permits a mixture of venous with arterial blood and accounts for cyanosis, but an intact alveolar surface eliminates sufficient carbon dioxide and hence dyspnea is absent. But let such a patient develop an edema of the lungs which interferes with carbon dioxide elimination and he becomes dyspneic at once. As Hoover has pointed out, this occurs in pulmonary edema from other causes. The frothy exudate in the bronchi if saturated by breathing pure oxygen becomes after a few minutes an oxygen foam and diminishes cyanosis. The carbon dioxide, meanwhile, is not carried off and dyspnea continues.

Again, in pneumonia a whole lung may be solidified, take up no oxygen, and thus as long as circulation in this lung continues, contribute venous blood to the arterial stream, thus causing cyanosis. The sound lung, however, is still able to eliminate sufficient carbon dioxide to prevent dyspnea. But let the sound lung become edematous and dyspnea appears.[3]

A large pleural effusion may throw one lung completely out of commission and yet no cyanosis may be present, because the completeness of the atelectasis shuts off the blood supply and hence no venous blood reaches the arterial stream.

Again, in chronic pulmonary tuberculosis there may be the most extensive pulmonary involvement with dyspnea but without cyanosis, because, again, the blood circulation is cut off at the same time as the alveolar function (Hoover).

It is perhaps unnecessary to recall the fact that anoxemia causes in the main a shallow and rapid respiration, whereas excess of carbon dioxide produces deep respirations. Cyanosis always indicates anoxemia, the hemoglobin being more or less reduced in quality, but anoxemia does not necessitate cyanosis. "In carbonic-oxide poisoning the blood is cherry red, and yet the patient may die for want of oxygen. Again, when carbonic acid is deficient the tissues may be suffering from anoxemia, and yet the blood may be red with hemoglobin, which will not part with its oxygen (according to Bohr's law) because of the lowness of the CO_2" (Rudolf).[4]

It must also be remembered that oxygen is carried to the tissues not only by the corpuscles but also by the plasma, and that the plasma content of oxygen can be greatly increased by raising the oxygen content of the respired air. This is one of the facts which helps to validate oxygen therapy.

Inhalation of pure oxygen by animals over prolonged intervals of time may be sufficiently irritating to set up a pneumonia. But as used clinically in human beings no such irritative action need be feared.

Pneumonia. Dyspnea in pneumonia may result from (1) pain, (2) extensive consolidation, (3) excessive bronchial secretions, (4) edema (usually cardiac) of the uninflamed alveoli, (5) pleural or pericardial effusion, (6) acidosis.

The conditions here are diametrically opposed to those encountered in late chronic pulmonary tuberculosis. In the latter instance the alveolar surface is gradually lost and the circulation in the involved portions is simultaneously occluded. Hence, the respiratory center accustoms itself to the gradual increase in the carbon dioxide tension of the blood, and, further, but little or no venous blood is contributed to the left heart by the lungs. In pneumonia the respiratory and circulatory mechanism is subjected to great

[3] Pearce, R. G.: Tr. Assn. Am. Phys., 1917, **32**, 71.
[4] Am. Jour. Med. Sci., 1920, **160**, 10.

and sudden abnormality, CO_2 tension is suddenly increased and unaërated blood passes from the diseased lung into the general circulation. The circulation of blood through the lung seems to vary with the stage of inflammation. During red hepatization it is, as a rule, fairly well preserved, but during gray hepatization most of the smaller arteries are occluded (Gross).

The respiratory center in pneumonia is depressed through a peripheral vagus mechanism,[5] its threshold of stimulation to carbon dioxide being less than normal. Hence, as shown by Pearce,[6] the carbon dioxide of the venous blood may be increased, although the alveolar carbon dioxide and the blood carbonates may be practically normal.

It has been suggested that the cyanosis of late pneumococcus pneumonia may sometimes be due to methemoglobinemia,[7] but Stadie's[8] investigations have shown that the degree of arterial and venous oxygen unsaturation varies greatly and that its amount is proportionate to the degree of cyanosis present. Further, that no unusually low total oxygen capacities are encountered even in fatal and intensely cyanotic cases, and hence no great degree of methemoglobinemia can exist. But inasmuch as most of his cases were of the influenzal type the possibility of methemoglobinemia as a cause of cyanosis in typical pneumococcus lobar pneumonia cannot be altogether denied.

Acidosis is another possible cause for dyspnea in pneumonia. As in other infections a mild degree of acidosis from metabolic changes may exist, but in addition it has been shown that acid production is an important bactericidal factor in the growth and death of the pneumococcus.[9] Hence, one wonders whether such acid production may be sufficient to alter the hydrogen ion content of the blood in sufficient degree to stimulate the respiratory center. During the febrile stage evidences of acidosis are often demonstrable by "increased ammonia and acid excretion, low carbon dioxide tension of the blood, diminished affinity of the blood for oxygen and the retention of large amounts of alkali." Peabody[10] found diminished carbon dioxide tension of the blood and Palmer and Henderson[11] increased ammonia and titratable acidity of the urine as well as increased alkali tolerance. However, Palmer's[12] investigations of pneumonia acidosis, as measured by the combined carbon dioxide in the plasma and the hydrogen ion concentration of the urine, indicate that such acidosis is seldom if ever severe. Hence, direct treatment of acidosis is rarely if ever necessary.

[5] Porter and Newburgh: Am. Jour. Physiol., 1917, **42**, 175.
[6] Tr. Assn. Am. Phys., 1917, **32**, 71.
[7] Butterfield and Peabody: Jour. Exper. Med., 1913, **17**, 97.
[8] Ibid., 1919, **30**, 215.
[9] Lord and Nye: Ibid., 389.
[10] Ibid., 1912, **16**, 701.
[11] Arch. Int. Med., 1913, **12**, 153.
[12] Jour. Exper. Med., 1917, **26**, 495.

Pain is in large manner responsible for shallow breathing, and this, as has been shown by Meakins,[13] may be an important cause of anoxemia. In these investigations it was found that with increasing respiratory rate there was a decrease in volume per respiration, but that the total minute volume was increased. There was, however, a "conspicuous diminution in the ratio between the volume of each respiration and the theoretical dead space." In other words, although the patient is breathing hard, pulmonary ventilation is poor. Here, too, a vicious circle may be established. Anoxemia produces shallow breathing and shallow breathing increases anoxemia. It is highly important, therefore, for this reason, as well as on account of the suffering and loss of sleep which it entails, to control pleuritic pain.

Pain is to be relieved by strapping, opiates, dry cupping or an ice-bag. The latter is often inadvisable in children, in the aged and in asthenic cases. We may also properly consider the fact that it may reduce temperature and that fever seems to bear a close, though as yet imperfectly understood, relation to the processes of immunization by virtue of which the crisis is induced. Some authorities bar the ice-bag for this reason even though its actual effect upon the reduction of temperature appears to be almost negligible.

Extensive consolidation as a cause of dyspnea is less easily combated. In sthenic cases, with a high venous pressure, phlebotomy is often advisable and cardiac stimulation indicated, digitalis being usually the most satisfactory drug. A copious supply of fresh air is essential.

Excessive secretions in the bronchi may result from concomitant bronchitis or from pulmonary edema. In the former instance aromatic spirits of ammonia or kindred drugs are useful; in the latter, digitalis and atropin are of proved merit, while epinephrin may be tried, especially if bronchial spasm be a contributing factor.

Pulmonary edema is a common late manifestation, not necessarily of marked and easily demonstrable degree, but simply as an excess of alveolar moisture which interferes to a greater or less extent with pulmonary ventilation by increasing the dead space.

Here, again, chief reliance must be placed upon digitalis and atropin, while phlebotomy and dry cupping may be considered. Massive *pleural* or *pericardial effusions* should be aspirated if edema threatens, or if by their size they interfere with pulmonary ventilation or heart action. In any of the foregoing conditions oxygen inhalation may be advisable. It is always indicated if anoxemia exists, and, as already stated, cyanosis always indicates anoxemia. The use of oxygen, as lately emphasized by Rudolf,[14] is certainly rational and has the forceful endorsement of no less an authority

[13] Arch. Int. Med., January 15, 1920.

[14] The Therapeutic Use of Oxygen, Am. Jour. Med. Sci., 1920, **160**, 10.

than Haldane, from whom I quote: "It may be argued that such measures as the administration of oxygen are at the best only palliative and of no use, since they do not remove the cause of the pathological conditions. As a physiologist I cannot agree with this reasoning. The living body is no machine, but constantly tending to maintain or to revert to the normal, and the respite afforded by such measures as the temporary administration of oxygen is not wasted but utilized for recuperation." But to be efficacious it must be properly administered, not by means of a funnel held near the patient's mouth, but by means of a rubber tube inserted into the nostril. Even its intermittent employment may spare the respiratory center as well as the other bodily tissues from the evil effects of anoxemia. The generally accepted teaching that pneumonia patients should be kept recumbent is usually correct; but occasionally obese patients with a more or less emphysema or those with cardiac lesions are much less dyspneic when propped up in bed.

Bronchial Asthma. Obstruction to expiration is greater than to inspiration. This increases the midcapacity and produces pulmonary distention. The diaphragm is forced down, which may interfere with the blood flow through the inferior vena cava. Diminished diaphragmatic excursion still further favors venous and lymphatic stasis. The amount of air breathed during an attack may actually be increased, but the dead space is also increased and hence little is gained by the added effort. Cyanosis indicates the degree of anoxemia. The spasm of the bronchioles and increased secretion are probably the results of a vagus stimulus. It has been suggested that the nervous center governing the bronchial muscles is hyperesthetic.

Asthmatic attacks are best controlled by epinephrin, atropin, morphin and benzyl benzoate. Counterirritation on the chest, neck or feet may be a useful adjuvant.

Recurrence may be prevented by the elimination of reflex causes, especially pathological conditions in the nose and pharynx.

Anaphylactic asthma may be cured if the offending antigen can be discovered. Hay fever asthma can be prevented if the proper pollen extract is administered. The rarer forms of anaphylactic asthma due to certain varieties of food are sometimes prevented by discovery and withdrawal of the particular protein in question. So also may those due to bacterial proteins by means of appropriate autogenous vaccines. In my experience, however, the results obtained from the last-mentioned two varieties have been discouraging.

In many cases no specific cause can be determined. It is only fair to state, however, that in many of these cases complicating factors, such as chronic pulmonary emphysema and fibrosis, anthracosis, arteriosclerosis, etc., have played a part.

Emphysema. In this condition pulmonary overdistention is usual and marked. One finds an increase in the midcapacity and an inability to properly ventilate the lungs, the residual air being increased. According to Bohr,[15] increase in the midcapacity in emphysema is essentially compensatory and facilitates circulation through the lungs. These views regarding the importance of physiological and pathological variations in the midcapacity have not been generally accepted. Diminution of the residual air, however, is of unquestioned importance and points toward a diminution of the alveolar surface. The vital capacity is decreased and the dead space increased. The increase of the dead space is not admitted by all observers. R. G. Pearce[16] attributes the high CO_2 figures to instrumental error and explains the cyanosis as resulting from a low oxygen content of the blood. According to this conception the low O_2 content of the diseased alveoli is not compensated by overventilation of the sound alveoli, because superventilation will not increase above the normal the absorption of O_2. Hence the oxygen tension in the blood leaving the heart will be low. The latter factor may be further magnified by the presence of moisture in the alveoli and the bronchi. This factor is indeed often the only one which is amenable to treatment. One cannot restore damaged alveoli nor their narrowed capillaries. It should be remembered also that the emphysematous subject not only requires more tidal air than a normal subject, but that the act of breathing itself is often so laborious that much carbon dioxide is thus produced. Further, that it is often impossible for him to increase his respiratory rate. The carbon dioxide tension in the alveolar air is abnormally high. The increased carbon dioxide content of the blood does not, however, produce its characteristic symptoms and sequelæ as promptly or at as low concentrations as it does in normal persons. This increased CO_2 tolerance by the emphysematous subject is in part due to an obtunding of the respiratory center and in part due to an increased value of the buffer substances in the body fluids (Scott).[17]

But little can be accomplished in controlling the dyspnea of emphysema. That moiety of the total which is due to asthma, bronchitis, edema or passive congestion may be amenable to treatment. Hence, digitalis, expectorants or atropin may be of value, as may also a change of climate. Hoover suggests that in emphysema with bronchitis, if cyanosis exists, but disappears under the inhalation of pure oxygen, we are justified in assuming that the anoxemia is the result of moisture in the air spaces and hence should expect beneficial results from a dry climate. If the patient remains unbenefited by the oxygen he will probably also remain unimproved

[15] Deutsch. Arch. f. klin. Med., 1907, **88**, 385.

[16] Physiology and Biochemistry in Modern Medicine, 1918, 311.

[17] Observations on the Pathological Physiology of Chronic Pulmonary Emphysema, Arch. Int. Med., 1920, **26**, 544.

by a dry atmosphere. Clinically it is common to find emphysematous individuals made worse by a visit to the seashore and improved by a trip to the mountains. Any factors tending to produce an acidosis should be vigorously combated, for the reasons already stated.

Pulmonary Tuberculosis. In early pulmonary tuberculosis the total and midcapacity of the lungs is usually normal while residual air may be increased. In moderately advanced and advanced cases the total capacity and midcapacity are decreased and residual air normal or increased. Dyspnea in this condition rarely calls for direct treatment except in the event of complications, such as massive effusions into the serous cavities or pneumothorax. These conditions will be considered elsewhere.

In advanced chronic cases, dyspnea, except upon exertion, is a late manifestation which usually results from widespread destruction of alveolar function. This is of such gradual occurrence and associated with coextensive and simultaneous obliteration of the pulmonary circulation that one is often surprised at autopsy to find how little sound tissue remains. Experimentally, one-sixth of the total lung volume is compatible with life as long as the animal remains at rest. In autopsies on tuberculous subjects what appears to be an equivalent destruction of tissue is often found. Dyspnea in advanced cases may result from coincident bronchitis, and when so may be relieved by appropriate treatment. Theoretically, heart weakness with passive pulmonary congestion may be a factor, but practically it rarely is so and digitalis medication is usually productive of little benefit. In the advanced cases some opiate gives the best results.

Pain resulting from pleurisy, by causing shallow breathing and increasing the dead space, may be a cause of dyspnea. This subject has already been discussed under the heading of Pneumonia.

Cough *per se*, by virtue of the effort it requires, may increase the demand for oxygen and increase carbon dioxide. Appropriate treatment tending to diminish cough is often efficacious. One naturally has in mind fresh air, voluntary inhibition or control, counterirritation, medicated inhalations, sedatives, expectorants, etc., and local treatment of the pharynx and tonsils.

Dyspnea may result from pulmonary hemorrhage; sometimes by actual reduction of oxygen-conveying corpuscles, often by obstruction of the air passages and by the fright and cough which accompany the bleeding. In such cases opiates stand first as a therapeutic measure while accessory measures such as mustard or heat to the feet and an ice-bag to the chest may bring additional benefit.

Pneumothorax. Localized pneumothorax is usually small, often unrecognized, except upon radioscopic examination, and from the standpoint of dyspnea, unimportant.

Total pneumothorax, on the other hand, especially if sudden in onset, produces marked dyspnea and often shock.

Dyspnea results not so much from the fact that one lung has ceased to functionate but as a result of displacement of the mediastinal viscera and interference with the expansion of the sound lung. In open pneumothorax nothing relieves dyspnea so well as closure of the wound, if this can be accomplished. In open pneumothorax due to pulmonary disease this often happens spontaneously as a result of pulmonary collapse or bronchial occlusion.

Experimental evidence indicates that the dyspnea in open pneumothorax is due not to the short-circuiting of a large quantity of blood through the collapsed lung but to imperfect alveolar ventilation of the sound lung by the mediastinal movements. The mediastinum moves toward the sound lung during inspiration and away from it during expiration, thus lessening the pulmonary ventilation (Hewlett). With the patient at rest all the factors of respiration, gaseous exchange, carbon-dioxide tension and the mechanical factors are normal in persons with a collapsed lung. Ventilation is normal despite the greatly reduced vital capacity as long as there is no demand, such as that entailed by exercise, for increased ventilation. Even the response to carbon dioxide is normal up to the point at which respiration is trebled.[18]

Aside from opiates and psychic control but little can be accomplished in relieving dyspnea in pneumothorax. If distress continues aspiration of air or fluid from the pleura may be tried as a palliative measure until the physiological readjustment has been established.

Pleural Effusion. Dyspnea, especially upon exertion, is often encountered. It is usually proportional to the size of the effusion and the degree of cardiac embarrassment.

Reserve air, complementary air and residual air are decreased, the first two factors named resulting from a low vital and total capacity. The midcapacity, although actually decreased, is normal in its percentage relation to total capacity (Peabody). The dead space increases as the lung becomes encroached upon.

Inasmuch as this type of dyspnea is grossly mechanical in origin, removal of fluid from the pleura is the obvious treatment to be employed. Transudates in the pleural cavity are closely associated with insufficiency of the right heart, and hence cardiac medication is often of primary importance.

Pulmonary Edema. The causes of this condition are various and sometimes multiple and the diseases in which it may occur are numerous. Its treatment will therefore in large measure depend upon the etiological factor. However, taking pulmonary edema simply as a symptom, the dyspnea of which calls for treatment, there are certain measures which are sufficiently rational and effective to justify employment in the average case.

[18] Means, J. H., and Balboni, G. M.: Jour. Exper. Med., 1916, **24**, 671.

Atropin sometimes alone, but more frequently combined with morphin, is often effectual, as is also digitalis. Dramatic improvement often follows phlebotomy, especially if venous pressure is high and the arterial pulse strong. If the edema be toxic in origin, as, for example, after phosgene inhalation, saline infusion should follow phlebotomy, for in these cases the blood becomes concentrated and the tissues oxygen-starved as a result of decreased volume. Whether a similar state of affairs exists in the spontaneous edemas of civil practice is, however, still a question for further study. One frequently encounters diminished respiratory function due to inadequate hemoglobin or erythrocytes in the blood, and it seems not at all unlikely that such a condition may be brought about by diminution in blood volume. In such event oral, rectal or intravenous saline therapy would be indicated. Until such treatment becomes effective, oxygen inhalations will tend to temporarily avert tissue asphyxiation. If the edema be obstructive in nature, and resulting from increased pressure in the pulmonary circulation, oxygen inhalation should follow bleeding.[19]

FURTHER OBSERVATIONS ON THE NATURE AND TREATMENT OF CHRONIC NEPHROSIS.

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In 1917 I published two papers,[1] [2] in which I proposed to separate from the chronic nephritides certain forms of chronic parenchymatous nephritis which have shown themselves, by certain clinical features and by investigations of the constituents of the blood, to be of a distinct variety resembling the so-called chronic nephroses. I also proposed at that time a rational method of treatment for such cases, directed particularly toward restoration of normal conditions in the blood. The new viewpoints which I thus advanced have aroused considerable discussion both here and abroad.

In a clinical lecture on "Renal Dropsy," delivered at the Addenbrooke Hospital in August, 1918, Sir Clifford Allbutt[3] speaks of the striking results obtained by my method of treatment in a case of chronic parenchymatous nephritis. Box[4] in an address before the Lambeth Division of the British Medical Association quotes a similar case and speaks highly of the beneficial results of "Epstein's

[19] Matsuoka, Y.: Jour. Path. and Bact., 1915, **20**, 53.
[1] Epstein, Albert A.: Am. Jour. Med. Sci., 1917, **154**, 638.
[2] Idem: Jour. Am. Med. Assn., August 11, 1917, p. 444.
[3] British Med. Jour., October 12, 1918, p. 395.
[4] Ibid., March 13, 1920, p. 356.

High Protein Diet." McCay[5] refers to a case of nephritis, with generalized edema, which was cured by the adoption of the "high protein diet." Symes[6] says, "We have found this diet to be most efficacious in reducing nephritic edema, and further than this, it has resulted in a marked improvement in the patient's general condition and in reducing the amount of albumin in the urine."

McLean and De Wesselow[7] discuss my method of dietetic treatment, which they have adopted for the treatment of their "hydremic cases," namely, those marked with edema and anasarca. They agree "that a high protein diet often results in removal of the dropsy in chronic nephritis is certain," but they differ from me in the explanation of the cause of the removal. I shall discuss this question later. Wordley,[8] without stating the source of his information, says "It is generally accepted that a rich protein diet is of value in the treatment of certain chronic cases with persistent edema, on the ground that the plasma protein, being low, will be increased thereby." His own position relative to this is somewhat inconsistent; he accepts the principle and rejects it at one and the same time. Although in his conclusions concerning the cause of the diuresis which follows the high protein diet in such cases, he inclines to the view of McLean and De Wesselow, yet by his own protocol (Case X) he furnishes a good illustration in my favor and proves by actual analysis that which he attempts to disprove by argument. I shall also discuss this later.

On the other hand, Kahn[9] in a series of 37 cases does not seem to be able to find any which correspond to the group described by me. In none could he discover a change in the protein composition or the lipoid content of the blood serum. He concludes his paper with the unwarranted statement that "The feeding of patients suffering with chronic parenchymatous nephritis on a protein-rich, fat-poor diet is rather a risky undertaking." No reasons are given. He ignores the fact that my treatment was designated for special cases with changes in the blood and urine of a specific type, the existence of which Kahn denies. It is therefore difficult to understand how he reached the above conclusion without the necessary experience.

In an editorial the *Journal of the American Medical Association*[10] discusses my views as well as the apparent inability of Kahn to find similar cases. It takes issue with his statement quoted above and concludes the discussion with the suggestion that "Clinical investigators should not abandon suggestions emanating from the

[5] Indian Med. Gaz., Calcutta, August, 1919, p. 54.
[6] British Med. Jour., April 10, 1920.
[7] Quart. Jour. Med., July, 1919, **12**.
[8] Ibid., 1920, **14**.
[9] Arch. Int. Med., 1920, **25**, 112.
[10] Jour. Am. Med. Assn., 1920, **74**, 19.

physiological laboratory without more conclusive assurances that they cannot apply to human disease."

Christian[11] in a paper in 1920, also in a chapter on subacute nephritis in *Oxford Medicine*,[12] where he quotes my dietetic treatment in detail, insists that he has not seen any beneficial results from it. His view coincides with that of Kahn as to the rarity of the group in which I have obtained such good results.

Geyelin too agrees with Kahn.[13] I will quote him in full in order to show the grounds upon which his views are based. He says: "My own experience during the past three years with cases of the type described by Epstein is in accord with that of Kahn. Bauman working in the wards of the Presbyterian Hospital has studied two patients who corresponded clinically to the Epstein type, and they both showed a high cholesterol content of the blood and a globulin to albumin ratio similar to those found in Epstein's cases. One case, a child, aged five years, had considerable edema, and an attempt to relieve this by high protein feeding resulted in gastro-intestinal disturbance and had to be abandoned. On a low salt diet this patient improved slightly.* In the second case the edema had largely disappeared on admission to the hospital, and continued salt restriction alone soon caused the remaining edema to disappear. Eight other cases clinically similar to those described by Epstein have been observed where salt and fluid restriction caused the edema to disappear. Unfortunately no blood protein or blood cholesterol determinations were made." He does not mention the total number of renal cases which he studied in the three years of which he speaks, yet he found 10 cases evidently belonging to my group. In only 2 cases was the blood examined by Bauman, and in both the results agree with mine. "Unfortunately" the remaining 8 cases were not examined as thoroughly as the others. In only 1 case out of the 10, therefore (that of a child), was a high protein diet instituted, and because of an upset stomach,† was discontinued.

This statement is very strange and incomprehensible, particularly when we compare it with the one made by Geyelin in another article published in a preceding number of the same journal.[14] "It is well recognized that protein restriction in certain forms of renal disease where there is no nitrogen retention, and when the blood-pressure is not high, is often carried to unnecessary extremes. No apparent effect is to be expected from protein restrictions under such conditions as mentioned, and in these cases a protein intake of 70 to 90 gm. per day is usually well tolerated, and is all the

[11] Jour. Am. Med. Assn., June 21, 1920, **74**, 615.
[12] Christian, H.: Oxford Med., vol. **3**, Chapter X.
[13] Prog. Med., December, 1920.
* It would be of interest to know the subsequent history of this case.
† Not an unusual occurrence in renal conditions.
[14] Prog. Med., 1919.

more permissible when the patient is under supervision and conditions are such as to permit of periodic estimations of the nonprotein nitrogen in the blood. In certain types of nephritis (Epstein) overfeeding of protein would seem to be indicated." It would be illuminating, on the basis of his own statements, to know just wherein Geyelin's experience agrees with that of Kahn.

In the above quotations we find, so far as I am aware, the existing expression of opinions, *pro* and *con*, concerning my views. The predominating opinion (though foreign) is favorable, and the objections raised by my colleagues in this country lack substantiation. The question of the nature and treatment of chronic nephrosis resolves itself into at least five distinct propositions, and disagreement with one or another of these does not affect the problem as a whole.

The propositions are: (1) That chronic nephrosis is a clinical and pathological entity; (2) that chronic nephrosis is essentially a metabolic disease; (3) that chronic nephrosis is characterized by definite changes in the protein and lipoid content of the blood serum; (4) that the water retention and consequent edema in this disease is of extrarenal origin and is due to reduced amount of colloid, and, hence, a lowered osmotic pressure of the blood; (5) that the feeding of large amounts of protein in the diet is the rational therapy for this disease. It may be added that cases of chronic glomerulonephritis with an intense and protracted albuminuria may at times show changes in the blood similar to those found in chronic nephrosis. In such cases the above findings constitute a late phenomenon, and the feeding of large amounts of protein in such cases may also be of benefit.

In the four years since the publication of my original papers (*loc. cit.*) I have had sufficient opportunity to test the soundness of my views. It seems to me, therefore, that it would be worth while to restate the matter in the light of further experience.

In order to clarify the type of case under consideration, and to which the high protein diet is to be applied, a few words concerning the subject of parenchymatous nephritis may not be out of place. Parenchymatous nephritis is the older term for certain groups of renal disease; it includes both the tubular and glomerular nephritis. The introduction of blood-pressure measurement in the clinic and of newer methods of blood chemistry in the laboratory have made it evident that this designation is unsatisfactory, for among the cases of parenchymatous nephritis there are at least two types which can be distinguished: (1) Those in which the glomeruli chiefly are diseased with secondary involvement of the tubules or interstitial tissue, or both, and which really represent an inflammation of the glomeruli—a glomerulonephritis; and (2) those cases in which tubular degeneration predominates or in which the glomeruli are not diseased. It was this consideration which

led Friedrich Müller to propose the term nephrosis for this second group of cases. Although the term nephrosis is not a happy one it has gradually been adopted by most writers in this field. In the newer monographs on renal disease, such as that of Volhard and Fahr,[15] Volhard,[16] Munk,[17] Richter,[18] etc., this term finds a definite place. This is rightly so, as it serves to separate (for the present at least) a group of cases which comply with special conditions. The newer studies on the blood chemistry and effusion fluids add support to the probable entity of this type of renal disease.

From the pathological standpoint, according to these authorities, chronic nephrosis is quite distinct. That the lesion in the kidneys in this condition is of an advanced degenerative type has been recently proved at autopsy.[19] From the similarity of the lesions to that produced by certain toxins and mineral poisons it is surmised that the disease (nephrosis) is due to an intoxication. Thus, for example, an acute tubular degeneration amounting in severe instances to tubular destruction is produced in poisoning of bichloride of mercury, bismuth, uranium, etc. Milder forms of parenchymal degeneration frequently occur in many febrile diseases, especially diphtheria, yellow fever and other infections. When the destruction of the tubular epithelium is not sufficient to produce death complete recovery takes place within a few weeks, as the tubules possess a remarkable capacity for regeneration. Although the kidney lesions in the acute and chronic forms of tubular nephritis (as just stated) may be alike, *it is questionable whether the cases which are encountered clinically, and which are termed "chronic nephrosis," ever actually result from an acute condition of the character described above.*

The true pathogenesis of this disorder must be left to the future to be determined. But many facts which we now possess strongly suggest that the disease begins as a metabolic disorder which leads primarily to the albuminuria (a diabetes albuminuricus), and secondarily to give rise to changes in the kidneys and to the other pathological and clinical sequelæ.

Chronic nephrosis is not a rare medical curiosity. Its frequency must be considerable, as allusions to the condition, by whatever term it may be designated, are numerous in the literature. Careful coördination of clinical data with chemical analysis of the blood and urine, however, is necessary for its recognition. Whether all cases of known etiology such as syphilis, tuberculosis and other general and focal infections and those of unknown causation are of the same order or not, the fact remains that cases of the type

[15] Die Brightsche Nierenkrankheit, Berlin, 1914.
[16] Die Doppelseitigen Haematogenen Nierenkrankungen, Berlin, 1918.
[17] Pathologie und Klinik der Nephrosen, Nephritiden und Schrimpfnieren, Berlin u. Wien, 1918.
[18] In Kraus's and Brugsch's System.
[19] Fahr: Loc. cit.

described by me exist and are fairly numerous. Munk[20] in speaking of "lipoid nephrosis," a type closely resembling mine, insists that the recognition of the entity of this condition is indispensable for a thorough clinical conception and the proper therapeutic management of this type of renal disease.

It is fair to admit that absolute standards for the differentiation of chronic nephrosis from the other types of "chronic parenchymatous nephritis" are still lacking, and it may at times be impossible to definitely place a given case until the therapeutic test (*i. e.*, a high protein diet) has been successfully applied. However, from our present knowledge the distinguishing features of chronic nephrosis are the following: The disease occurs in relatively young individuals. It is of obscure or unknown origin and bears no definite relation to known infectious diseases. In some instances pregnancy may stand in etiological relationship to the condition. Objectively it is characterized by a pronounced albuminuria with or without casts. The urine is usually free from blood elements. The blood-pressure is not elevated. At first the condition may be devoid of other gross manifestations; subjective symptoms may also be lacking and the exact time of onset frequently cannot be determined. Its development may be slow and insidious, but as it progresses oliguria and edema invariably develop. Pallor is usually very pronounced (the skin is of a dirty gray or putty-like color), and together with puffiness of the eyelids or swelling of the ankles may be the first symptoms to attract the patient's attention. Loss of appetite and a feeling of fatigue may be among the earlier symptoms. Headache, vomiting and diarrhea may also be present. Pain in the back may be encountered as a symptom, but not very frequently.

As stated above, with the progress of the disease the edema becomes marked. It reaches its highest degree in this disease and forms the chief clinical manifestation. Of great importance, also, is the state of the cardiovascular system. The heart is not enlarged, the blood-pressure is normal and in uncomplicated cases is never increased.

The urinary picture is characteristic. The quantity is much reduced, of a high specific gravity and contains large quantities of albumin.* In my previous papers (*loc. cit.*) I stated that the daily output for weeks and months may amount to as much as 50 gm. a day. In the earlier stages the output of urinary excretory substances may be normal, but functional tests show renal deficiency, such as retention of chlorides, of nitrogen and diminished phenolsulphonephthalein excretion. Water retention may also occur in the early preëdematous stages of the disease. The body

[20] Loc. cit.

* According to Munk, lipoid substances are present in the urine and can be readily detected microscopically.

tissues (other than subcutaneous) are evidently capable of storing up considerable fluid before showing definitely the presence of edema.[21] In fully developed cases the retention of chlorides and of nitrogen (as measured by test diets) may be quite marked, and yet the blood may fail to give evidence of such retention. This is particularly true in the edematous stages of the disease. The condition is not at all paradoxical. An explanation for it can be found in the greater distribution of the retained substances throughout the body in the water-logged tissues. In my earlier publications,[22 23 24] I have drawn attention to the fact that the non-protein constituents of effusion fluids approximate those of the blood in the same cases, both in point of quality and quantity. Denis and Minot[25] have also recently found that the non-protein constituents of the fluids (which belong to the class of crystalloids and among which are urea, uric acid and creatinin) occur in the same concentration in exudates and transudates as in the blood. They have also found that the concentration of the non-protein substances in ascitic fluid, for example, is easily influenced by diet. That the absence of increased concentration of the non-protein nitrogenous substances in the blood in cases of nephrosis is probably due to increased distribution of these substances throughout the body (or dilution) is further evidenced by the fact that both in the early preëdematous as well as the postedematous stage (following treatment and general improvement) increased concentration of nitrogenous waste products as well as chlorides occurs. It may be added here, for the reasons stated, that estimations of soluble substances in the blood, in all cases associated with massive effusions or edema, do not accurately measure the quantity of such substances which are retained in the body. This is of importance in the interpretation of functional tests of the kidney.

Apart from the characteristics mentioned and from the clinical manifestations there occur in the blood certain changes which seem to distinguish this group from every other form of renal disease. These changes may be placed under two headings, primary and secondary.

As a primary change I consider the increase in the lipoid content of the blood. Of the lipoid substances it is cholesterol which has been especially studied. I called attention to this in my previous publications. Normally, cholesterol occurs in the blood as free cholesterol and as an ester, together varying from about 0.175 per cent to 0.225 per cent. Slight variations may occur in other forms of renal disease. But in the cases under consideration

[21] Epstein, Albert A.: Medical Clinics of North America, July 1920, **4**, 145.
[22] Idem: Loc. cit.
[23] " Loc. cit.
[24] " Jour. Exp. Med., 1912, **16**, 719; 1913, **17**, 444; 1914, **20**, 334.
[25] Arch. Int. Med., 1917, **20**, 879.

the most marked increase has been noted. In my former publications I gave figures ranging from 0.333 per cent to 1.23 per cent. In other renal conditions, including surgical diseases, no such increase occurs. Occasionally a moderate rise may be encountered, but as a rule, this is associated with some other superimposed condition. Of interest, also, is the fact that in uremic cases, in those particularly showing a high nitrogen retention in the blood (the dry or so-called azotemic cases), the lipoid content is very much diminished. The cholesterol in such cases may fall as low as 0.06 gm. per 100 cc of blood. This is in conformity with the observations of Chauffard, Laroche and Grigaut.[26]

A milky appearance of the serum of certain nephritics was observed also by the older writers, notably by Bright[27] and also by Rayer.[28] However, careful chemical analysis of the blood in such cases has been made only in relatively recent times. In 23 cases of severe nephritis which Bloor[29] examined, the blood cholesterol values were practically normal. None of his cases were clinically of the type under discussion. In only one instance (Case XV, E 223) was edema present, and that was one of acute nephritis. Denis[30] found an increased cholesterol content in the blood in only 1 of 50 cases (Case C 253). This case is the only one in her series which might be called a "chronic parenchymatous nephritis." The first blood examination in this case yielded 0.475 per cent cholesterol and a second examination after a short interval showed 0.606 per cent cholesterol. Müller[31] found 0.84 per cent cholesterol in the blood in a case of nephritic lipemia. In a series of cases observed by Widal, Weill and Laudat[32] moderate increases in the blood cholesterol were found in a number of instances, but the highest value, 1.08 per cent, was obtained in a case associated with a very intense albuminuria. Beumer[33] found an increase in the cholesterol of the blood serum of nephrotic patients but not in other nephritides. Stepp[34] studied the cholesterol content of the blood in different forms of Bright's disease and found that in all cases of severe injury to the kidney parenchyma an increase in the cholesterol content of the blood occurred. On the other hand, types of nephritis in which interstitial change predominated did not show such increase. My own further observations only confirm the earlier ones. The cholesterol of the

[26] Compt. rend. Soc. de biol., 1911, **70**, 108.
[27] See reference. [22]
[28] See reference. [22]
[29] Jour. Biol. Chem., 1917, **31**, 575.
[30] Ibid., 1917, **29**, 93.
[31] Physiol. Chem., 1913, **86**, 469.
[32] Semaine méd., 1912, **32**, 529.
[33] Monatschr. f. Kinderh., 1920, **18**; abstract, Jour. Am. Med. Assn., **75**, 1300.
[34] Deutsch. Arch. f. klin. Med., 1918, **127**, 439–467.

blood has varied in the later series of cases from 0.3 per cent to 1.3 per cent.*

The increase in the lipoid content of the blood of chronic nephrosis constitutes a fundamental change and is of primary importance. It is undoubtedly of greater significance than is the lipoidemia of diabetes. In the latter disease it occurs occasionally as a result of an excessive absorption and a perverted utilization of fat, and is frequently associated with an acidosis. Although the origin of the lipoidemia in nephrosis is still obscure it is unquestionably of a different order from that which occurs in diabetes mellitus. If the lipoidemia of chronic nephrosis were due to the accumulation resulting from ingested fat, restriction of fat should cause a fall in the lipoid content of the blood; but that is not the case. The mere elimination of fat from the diet does not influence the lipoidemia of chronic nephrosis to any great extent. We must therefore ascribe this lipoidemia to other sources—in part, perhaps, to the mobilization of body fat, particularly as such cases show extreme emaciation when recuperation occurs. Tissue degeneration may also contribute its quota of lipoid material to the blood (Koch and Voegltlin).

Like the albuminuria the lipoidemia is a constant accompaniment of chronic nephrosis, and, in a measure, serves as an index of the degree of the severity of the disturbance. The inability of some investigators to find it can be accounted for only by the absence of appropriate cases (Bloor and Denis), or by the fact that their observations were based, in all probability, on cases of diffuse glomerular nephritis in which the lipoid content is not necessarily increased (Kahn).

No reasonable explanation of the lipoidemia can be found unless we assume that chronic nephrosis represents a specific type of disordered metabolism. That this deduction is warranted seems supported by the fact that in certain instances a hypothyroid state is definitely demonstrable. Basal metabolism has been found to be decreased where such studies have been made.[35] These studies have convinced me that we have a series of borderline cases on one side of which there are cases with a clinical picture of nephrosis and on the other side cases with distinct hypothyroidism and "frustes" forms of myxedema.†

As a secondary change I consider the reduction of the protein in the blood serum and the change in the ratio of albumin to globulin. Of these the change in the ratio of albumin to globulin is

* By far the largest number of blood analyses for cholesterol have been made by my colleague, Dr. Joseph Reiss. Other members in the staff of the physiological department have contributed to this work. To all of them, and particularly to Dr. Joseph Reiss, I wish to extend my thanks for unselfish coöperation.

[35] Aub, J. C., and Du Bois, E. F., and Soderstrom, G. F.: Arch. Int. Med., May, 1917, p. 865.

† This will form the subject of a future report by the author and Lande.

possibly of greater importance than the reduction of total protein. In many cases it is the earliest manifestation. In my previous publications I gave figures for the normal and the changes occurring in the cases of nephrosis. Normally the protein of the blood serum forms about 6 to 8 per cent while the ratio of albumin to globulin is about 4 to 2 or 5 to 3, *i. e.*, the globulin forming about 37 per cent of the total protein. In nephrosis in my previously reported cases I found the figures for the total protein of the blood serum to average 3.928 per cent and the ratio of albumin to globulin to average 0.466 per cent of albumin to 3.426 per cent of globulin, the globulin forming 89.2 per cent of the total protein. Since then investigation has corroborated the above figures.

The reduction in the protein content of the blood serum is of twofold importance: (1) It stands in causal relationship to the edema, and (2) it furnishes an intimation to the effect of the albuminuria on the nutrition of the body, thus pointing a way to a rational therapeutic measure.*

To summarize: We have then in the case of nephrosis a clinical picture characterized by a gradual onset, a protracted course, edema, anasarca and effusion of the serous cavities; by oliguria, marked albuminuria and occasional cylindruria, a high specific gravity which indicates ability to concentrate the urine. It is also characterized by the absence of any increased blood-pressure and any cardiac hypertrophy and by the absence of any marked nitrogen-retention in the blood. It is also characterized fundamentally by a marked increase in the cholesterol content of the blood, by a reduction in the total protein of the blood serum and by the inversion of the normal ratio of albumin to globulin. The whole presents a metabolic disturbance of nutrition. It is more pronounced in younger individuals. It stands in all probability in some relationship to states of hypothyroidism.

The above characteristics typify the pure forms of chronic nephrosis. Unfortunately renal diseases do not often pursue a clear-cut course. Undoubtedly there occur cases of glomerulonephritis to which the pathological picture of nephrosis is added, and *vice versa*. I have cited a case of the latter type in my article in the *Medical Clinics of North America*.[36] In practice they are common. The separation of the individual elements may at times be difficult. However, increase in the blood-pressure, a marked nitrogen retention and the presence of any blood in the urine

* The use of the refractometer for the determination of the total protein or the globulins in the blood serum of cases of chronic nephrosis is inadvisable. The marked lipoid content which is found in such sera interferes with the accurate reading for the protein. In fact the lipoids may interefere even with other methods of analysis, such as the precipitation of the globulins by means of ammonium sulphate. Where a marked lipoidemia is present it is necessary, therefore, to treat the serum first with ether, removing the ether by ventilation, precipitation of the globulins occurs, then, without any interference from the lipoids.

[36] Epstein, Albert A.: Loc. cit.

point to the glomerulonephritic element. Increase in the cholesterol, reduction in the protein and change in the albumin-globulin ratio in the serum point to the nephrotic element. It is of importance from the therapeutic standpoint to separate these elements, for with the abeyance of the glomerular inflammation treatment should be directed along the same lines as those indicated in cases of nephrosis. This will be discussed later. Numerous reasons exist for the belief that chronic nephrosis, or a renal disturbance closely resembling it, is a metabolic disorder from the beginning to the end. Nevertheless it is possible that certain of the phenomena which seem to characterize chronic nephrosis may occur in other types of renal disease and may be secondary to inflammation of the kidney. I refer particularly to cases of true nephritis which are accompanied by protracted albuminuria of a severe grade. Whether the albuminuria is the result of a general metabolic disturbance or the product of an inflammatory process in the kidney is quite immaterial as regards its ultimate effect on the blood. The relation between the albuminuria and the protein composition of the blood serum is a direct quantitative one. The more intense the albuminuria the greater will be the loss of serum protein (unless that loss is replaced somehow) and the more profound will be the effect on the general nutrition of the body. Whether the severe loss of protein substance can produce a lipoidemia also is a question which our present knowledge does not answer.

The fundamental point in the therapy of such cases is the loss of proteins in the urine and the consequent impoverishment of the blood in these substances.

The question has been raised by some observers as to the efficacy of the high protein diet in the treatment of the disease under discussion. Before advancing a rational therapeutic measure which should aim at the improvement of the fundamental chemical changes it is necessary, of course, for us to investigate how far these changes are responsible for the symptoms which objectively present themselves. Of these the most important one is the edema.

Since the time of Bright explanations for the cause of renal edema have been manifold. The modern theories may be classified under three headings: (1) Edema is the result of the inability on the part of the kidneys to excrete certain substances, such as water (Koranyi) and salt (Widal, Strauss, etc.). (2) Edema is the result of some injury to the capillary and endothelial walls: (*a*) As a result of an inflammatory condition (Cohnheim, Senator); (*b*) as a result of abnormal toxins due to destruction of the kidney cells, nephrolysin (Ascoli). (3) Edema is the result of some change in the tissues: (*a*) A colloid chemical change (Fischer); (*b*) a diminution of the elasticity of the subcutaneous tissues (Landerer).

It would lead us too far to attempt to examine in detail the basis for all these various theories. Just a cursory review is necessary to show their inadequacy:

1. The theory that edema is the result of the inability of the kidneys to excrete certain substances is at first glance very attractive when we notice the diminution of urine with the appearance of the edema. Koranyi and his pupils attempted to explain renal edema on the basis of the inability of the kidney to excrete water and the consequent water retention eventually resulting in the accumulation of fluid in the tissue spaces. That this explanation is not adequate is at once seen when we consider the cases of chronic glomerulonephritis with kidney insufficiency. We find here, according to some authorities, a marked hydremia, and yet these cases run, as a rule, until the end without any edema while cases of nephrosis with marked edema do not show any real hydremia.

Widal,[37] Strauss[38] and others believe the cause of edema to be the inability of the kidney to excrete salt. The retention of salt necessitates the retention of water to hold it in physiological solution. Widal's explanation is based especially upon the experiment of Widal and Javal on a case of renal edema, where they promptly produced edema four times by feeding the patient salt and by having first caused the edema to disappear by withdrawing the salt.

There is no doubt whatsoever that withholding the salt will in many cases (more particularly cardiorenal types) reduce the edema, and even cause it to disappear, but that the retention of salt is the underlying cause of the edema cannot be accepted. In cases of complete suppression of urine salt is retained with the other substances of excretion; here the concentration of the salt in the blood may reach to above 1 per cent without the production of edema. In chronic interstitial forms of nephritis (in hypertensive forms) retention of salt occurs but no retention of water.

2. The theory that edema is the result of an increased permeability of the capillary endothelial cell has its origin with Cohnheim. He assumed an inflammatory condition of the capillaries of the skin which caused this increased permeability. He was followed by Senator,[39] who assumed that the edema is not a consequent but a parallel phenomenon of the nephritis and due to injury of the capillary wall by the same toxin that caused the nephritis. This theory of increased permeability of the capillary endothelial wall seems to have found more favor with many of the modern writers on kidney disease.

Volhard[40] as well as Richter[41] subscribe to this theory, although they do not accept the idea that the injury to the capillary wall is an inflammatory one.

[37] Bull. et mém. Soc. méd. d. hôp. de Paris, June 12, 1902.
[38] Die chronischen Nierenentzündungen, etc., Berlin, 1908.
[39] Lehrbuch der Nierenkrankheiten, Wien und Leipzig.
[40] Loc. cit.
[41] Loc. cit.

Against the theory of the inflammatory condition of the capillaries we have the fact that the edema of cases of nephrosis is not of an inflammatory character. In a previous paper[42] I have shown that the edema fluid in these cases is made up principally of salt and water and that it contains only a trifling amount of protein. Against the view of Senator is also the fact that glomerulonephritis occasionally runs its course without any edema. Moreover, recent observations in experimental nephritis show that capillary permeability is diminished and not increased.[43]

Ascoli[44] assumes that during the course of nephritis, toxic substances and "nephrolysins" are produced which injure the endothelial cells of the capillary. This has received support from the fact that some observers have found substances with a lymphagogue action in the serum of the blood and edema fluid in cases of nephritis (Kast, Sterling). No definite nephrolysins have, however, been isolated, and the assumption of Ascoli is purely hypothetical.

3. These theories are based on the assumption of some change in the tissues. Of these, Fischer's colloid chemical theory has aroused much notice. Fischer assumes an increased imbibition of the tissue colloids under the influence of an increased avidity of the cells. This theory is not acceptable for many reasons, a few of which stand out prominently. An increased avidity of the tissue cells for fluid would not account for the presence of fluid between the cells which constitutes edema. Also, it has been shown that the tissues in edema are not abnormally acid and that an increase in acidity sufficient to cause a marked imbibition of the tissue colloids would result in the death of the tissue.

Landerer[45] assumed the edema to be due to a diminished elasticity of the tissues, but Boenninger[46] points out the objections to this. In old people with loose skin the elasticity is undoubtedly reduced, and yet no edema results. The same is true of the lax tissues which persist in cases after resorption of the edema.

From the review of these theories it will be seen that although they are many and varied, yet they do not offer a reasonable explanation. It is necessary therefore before attempting to explain the causes of edema to discuss the principles underlying the formation of lymph and tissue fluid. We must distinguish between the various forms of fluid which together are often termed "lymph." First, there is the transudate which leaves the circulation through the capillary wall and which contains all of the nutrition material necessary for the cell. Then the tissue fluid which contains some of the transudate but mixed with it—some of the waste products

[42] Epstein, Albert A.: Loc. cit.

[43] Chisholm, Boycott and Douglas: Jour. Path. and Bacteriol., 1914, **19**, 265. Bogert, Underhill and Mendel: Am. Jour. Physiol., 1916, **41**, 189.

[44] Vorlesungen über Urämie, Jena, 1903.

[45] Die Gewesspannung, etc., Leipzig, 1884.

[46] Ztschr. f. exp. Path. u. Therap., 1, 8. a.

of cell metabolism. Finally, there is the fluid which is contained in the lymphatic vessel or lymph proper.

The tissue fluid serves as a middleman between the circulation and the tissue while the lymph serves the purpose of removing any excessive transudate as a result of increased cell activity. This is shown best in the case of glandular activity such as that of the salivary glands, and better still in the case of the liver. Increased liver activity at once increases the transudate, and as a consequence the lymph flows from that organ, and, following this, from the thoracic duct.

Normally a satisfactory balance is maintained between the amount of transudate, tissue fluid and lymph flow. It is maintained at a low level of activity in the case of the resting limbs and at a higher level of activity in the case of the glandular organs.

What are the forces, then, which maintain this balance? What causes a disturbance of this balance, and with what result?

In this field, as in that of the kidney, the dispute has been between those who believe in the active secretion of the endothelial cell of the capillary wall and those who believe in filtration through the capillary wall. Modern physiologists, as Starling,[47] assume the endothelial cell to act as a filtering membrane of variable permeability, and that the factors responsible for the transudations are of two classes: (1) Mechanical, depending upon pressure in the capillaries; (2) chemical, depending upon the constituents of the blood and tissue fluid and upon the processes of diffusion and osmosis. By the term variable permeability is meant the condition of the capillary wall in various parts of the body which vary in regard to completeness. This is again best illustrated in the case of the liver, where the capillary endothelial lining is discontinuous—that is, the capillaries lack a complete endothelial wall. The capillaries of the intestines are less permeable than those of the liver, but more so than those of the limbs. In the intestine and in the liver, therefore, an increase in the capillary pressure will at once cause an increase in the transudate and in the flow of lymph (Starling).[48]

Although both factors, the mechanical and the chemical, are concerned in every part of the body, the chemical factor comes into more play in the limbs where the capillary wall is less permeable than is the case in the liver or in the intestine. Their interchange between the blood and tissue fluid is dependent not only upon filtration but also upon the osmotic forces of the dissolved substances. Here the breaking-down of large molecules into smaller ones in the process of muscular activity increases the number of molecules with the consequent increase in osmotic pressure in the tissue fluid. This causes an increase in the transudate from the

[47] Principles of Human Physiol., Philadelphia, 1920.
[48] Loc. cit.

blood—that is, in the flow of fluid from the lower to the higher concentration. The opposite is true when the blood becomes more concentrated, such as after an injection of dextrose which results in the flow of fluid from the tissue to the blood.

We have therefore normally these forces of intracapillary pressure and of the osmotic force, of the dissolved substances, normally balancing each other to maintain a constant interchange between the blood and the tissues, and varying with the activity and the demand of the tissues.

Anything, therefore, which causes a change in the intracapillary pressure or in the osmotic pressure, concentration in the dissolved substances will at once cause a disturbance in the tissue fluid. A simple illustration of the result of changing the intracapillary pressure is the effect of hemorrhage. This is at once followed by a universal fall in the capillary pressure below that of the surrounding tissue fluid, and this results in the backward filtration which makes up for the loss of the fluid.

Increase in the intracapillary pressure must be equalized by a corresponding increase in the osmotic concentration of the blood, and if this does not occur is followed by an increase in the amount of the transudate; and if the increased amount of transudate is not promptly removed, accumulation of fluid in the interspaces will result (cardiac decompensation, hepatic cirrhosis and localized inflammatory processes).

If the intracapillary pressure is not effected but there is an increase in the osmotic pressure in the blood, there will be an increased absorption of fluids from the surrounding tissues into the blood stream with resulting dryness of the tissues. This is the case in diabetes with a high sugar content in the blood. Again, if the osmotic pressure of the blood sinks this will remove the counterbalance of the normal intracapillary filtering pressure, and the result will be an increased transudate and increased accumulation of fluid in the interspaces.

With these principles in mind we may attempt an explanation of edema.

The characteristic of renal edema fluid which distinguishes it from the fluid of cardiac, or static, or obstructive edema is the low protein content. This may be as low as 0.1 per cent, whereas in the case of cardiac edema the protein content of the fluid is much higher. This also distinguishes the nephrotic edema from the edema of glomerulonephritis, where the protein content of the edema fluid is also higher. Recently, Beckman[49] found the edema fluid in tubular disease of the kidney to contain protein generally under 0.1 per cent; the highest protein content he found in glomerulonephritis.

[49] Deutsch. Arch. f. klin. Med., 1921, **135**.

These types of edema—namely, cardiac, nephritic and nephrotic—can be distinguished, therefore, by their protein content. They are also produced differently.

Cardiac edema is the result of relative myocardial insufficiency. The diminution of the volume output of the heart causes a slowing of the venous blood flow, a stasis with enormously increased capillary pressure. The balance between the intracapillary pressure and the osmotic force of the blood is disturbed in favor of the intracapillary pressure, and the result is increased filtration, with an increase in the transudate, not varying a great deal in its constitution from that of the blood plasma. Cardiac edema occurs especially in the dependent portions of the body where the pressure is greatest.

The edema of glomerulonephritis is also probably due to increased capillary pressure with increased filtration. Here the edema is generalized because the increase in the capillary pressure is general and is due to the increase in the blood-pressure with narrowing of the capillaries all over the body. With the method elaborated for observing skin capillaries under the microscope by Weiss[50] and others, it has been found that in acute glomerulonephritis with increased blood-pressure the blood in the capillaries did not flow evenly, but that the flow was interrupted and the capillaries narrow and elongated (Volhard).

The edema of nephrosis is also due to a disturbance in the balance between the intracapillary pressure and the osmotic force of the blood. But the fault here is with the osmotic force. According to the investigations of Starling the proteins of the blood exert an osmotic pressure of 25 to 30 mm. of mercury. In my paper concerning the causation of edema in chronic parenchymatous nephritis[51] I advanced the theory that it is the loss of protein through the urine which causes the diminution of the osmotic force of the blood: That this leads to a disturbance in the balance between the osmotic force and the intracapillary pressure, and by virtue of this the osmotic power of the tissue fluid at the same time becomes relatively increased, resulting in the attraction of fluid from the blood to the tissue fluids. I stated, then, that the loss of protein from the blood serum is sometimes equivalent to from 60 to 70 per cent of the total. "In terms of osmosis this loss of protein represents a pressure equal to 20 to 24 mm. of mercury, a factor sufficient to disturb the equilibrium in the exchange of fluid between the blood and the tissues. . . . More precisely the deficit in the serum protein causes a fall in the osmotic pressure of the blood. This disturbance does not only favor the passage of fluid from the blood to the tissues but also gives to the tissues the controlling power to absorb and retain fluid."

[50] Deutsch. Arch. f. klin. Med., vol. **119**, S. 1.
[51] Epstein, Albert A.: Loc. cit.

The above theory that edema is due to a loss of protein from the blood serum has received added support by the study of the so-called "war edema," and by experimental production of edema.

War edema began to appear in the Central European States in 1915. Those who studied it noticed the resemblance of the disease to what had been described in previous wars under different names. Bigland[52] observed edema in Turkish prisoners of war in Egypt. He noticed its resemblance to what had been called "epidemic dropsy" in India and to the edema observed in South Africa. Jansen[53] made extensive studies concerning the pathogenesis of this disease. His studies are of extreme interest, for they show conclusively that the edema is the result of loss of protein to the body through insufficient nutrition. His cases showed a distinct diminution of the protein in the blood serum. I quote from Table VIII, page 171:

There were found:

In 10 investigations	8.5 to 6.5 protein, normal.
In 10 investigations	6.4 to 6.0 protein, subnormal.
In 16 investigations	5.9 to 5.0 protein, much diminished.
In 4 investigations	4.7 to 4.0 protein, very much diminished.

Falta[54] also ascribes the war edema to insufficient protein in the food. The experimental studies of edema by Denton and Kohman[55] and by Kohman[56] have shown the importance of protein in the production of edema. They caused the appearance of edema in animals under protein undernutrition. On feeding carrots only to young rats a number of the animals developed edema. When part of the diet was replaced by protein, such as casein, the edema did not appear.

From the above it can be seen that the theory of edema advocated by me does not only seem plausible, but is gradually becoming solidly established. Still more support is supplied by the effect obtainable from a proper therapy in cases of chronic nephrosis (Albutt, Box, Syms, McLay, McLean and De Wesselow and Wordley).

Based on the above reasoning and conclusions I have proposed in my previous publications[57] a rational dietetic treatment. This consists in the feeding of a high-protein, fat-free, carbohydrate-poor diet. The protein is to replace the protein lost by way of the urine so as to increase the osmotic force of the blood. This, of course, does not occur by direct reëntry of the ingested proteins

[52] Lancet, January 3, 1920, p. 243.
[53] Deutsch. Arch. f. klin. Med., 1919–1920, **131**, 144.
[54] Wien. klin. Wchnschr., 1917, S. 1637.
[55] Jour. Biol. Chem., 1918, **36**, 249.
[56] Proc. Soc. Exper. Biol. and Med., 1919, **16**, 121; Am. Jour. Physiol., 1920, **51**, 185.
[57] Epstein, Albert A.: Loc. cit.

into the blood but by furnishing the necessary building blocks for the reconstruction of the protein lost from the body. The fat-free, carbohydrate-poor part of the diet is to compel the body to utilize the protein as well as the lipoids which are present in the blood stream. The diet has been very efficient in my hands, and in the hands of others also, as indicated from the results mentioned in the beginning of this paper.

It has been supposed that protein feeding increased the albuminuria of nephritis. In my previous publications[58] I have drawn attention to the fact that protein feeding has no such effect. Eichhorst[59] claims that the protein in the diet does not affect the albuminuria one way or another. More recently Wordley[60] made observations on this point and arrived at the same conclusions.

McLean and De Wesselow,[61] who had good results with the high protein diet, ascribed the removal of the edema not to the increase of the protein in the blood but rather to the increase in urea as a result of the breaking down of added protein. As evidence they cite the increase in the urea content of the blood and the well-known diuretic action of urea. In answer to this it may be said that the increase in the urea content of the blood may as well not be the cause of the disappearance of the edema but rather, and in all reason is, the result of the edema fluid being reabsorbed into the blood stream preparatory to its elimination by the kidney. As the edema fluid is reabsorbed in response to the osmotic force of the increased protein in the blood it carries with it the urea which it contains. As the urea in the blood and in the edema fluid are in osmotic equilibrium the urea in the blood cannot exert any osmotic pressure, to which McLean and DeWesselow partly ascribe the removal of edema.

I have referred to the work of Denis and Minot,[62] which shows the effect of feeding protein on the non-protein composition of ascitic fluid. Being evenly distributed in the blood stream and the tissue fluid the urea cannot be said to possess an osmotic pressure favoring the passage of fluid in one direction or another, so that the disappearance of the edema cannot be ascribed to that cause. As for the effect of the urea as a direct diuretic, definite evidence is lacking. The persistence of an elevated non-protein nitrogen content in the blood in some cases, long after subsidence of the edema, shows the lag on the part of the kidneys to eliminate the nitrogenous waste products as contrasted with the prompt elimination of water.

Wordley[63] holds to the same opinion about the cause of the removal of edema as do McLean and De Wesselow, yet in his

[58] Epstein, Albert A.: Loc. cit.
[59] Eichhorst: See references [1] and [2].
[60] Loc. cit.
[61] Loc. cit.
[62] Loc. cit.
[63] Loc. cit.

Case X the evidence is strongly in my favor. I cite his figures in detail:

CASE X.

No. of experiments.	Protein per cent.	Diet.	Remarks.
1	2.427	Fish	Feels fairly well; edema increasing.
2	2.328	Fish	Blood urea, 94 mg. per 100 cc; plasma protein, 5.06 per cent; multiple punctures of legs performed.
3	1.76	Milk	Draining freely from punctures.
4	1.456	Milk	Stopped draining.
5	1.988	Milk	Less edematous.
6	1.756	Milk	Plasma protein, 8.2 per cent; blood urea, 52 mg. per 100 cc; urinary chlorides, 0.23 per cent; is much better.
7	2.06	Fat and carbohydrate salt-free.	
8	1.84	Fat and carbohydrate salt-free	Slightly more edematous.
9	2.068	Fat and carbohydrate salt-free	Much more edematous; drain with Southey tubes; urinary chlorides, 0.076 per cent.
10	2.8	Fat and carbohydrate salt-free	Still draining; intensely edematous; much worse.
12	2.5	Fat and carbohydrate salt-free	Blood urea, 198 mg. per 100 cc; plasma protein, 4.57 per cent.
13	2.18	Fat and carbohydrate salt-	Tremendous edema; moribund.

It will be seen from the above that with the improvement of the edema the plasma protein increases from 5.06 per cent as noticed in Experiment 2 to 8.2 per cent as noticed in Experiment 6. Again it will be noticed that the improvement occurred when the patient was on a fish diet, and that when put on a fat and carbohydrate diet, which was also salt-free, the edema increased to a marked degree, and at the same time the plasma protein sank to 4.5 per cent as noticed in Experiment 12. This case is a beautiful illustration of the relation of the plasma protein to the causation of edema.

The diet that I employ is the same one that I evolved in my previous publication.[64]

DIET EMPLOYED.

	Daily amount.
Food value	1280 to 2500 calories
Proteins	120 to 240 grams
Fats (unavoidable)	20 to 40 "
Carbohydrate	150 to 300 "

[64] Epstein, Albert A.: Loc. cit.

into the blood but by furnishing the necessary building blocks for the reconstruction of the protein lost from the body. The fat-free, carbohydrate-poor part of the diet is to compel the body to utilize the protein as well as the lipoids which are present in the blood stream. The diet has been very efficient in my hands, and in the hands of others also, as indicated from the results mentioned in the beginning of this paper.

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Food value	1280 to 2500 calories
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Fats (unavoidable)	20 to 40 "
Carbohydrate	150 to 300 "

[64] Epstein, Albert A.: Loc. cit.

Articles of Food Used. Lean veal, lean ham, whites of eggs, oysters, gelatin, lima beans, lentils, split peas, green peas, mushrooms, rice, oatmeal, bananas, skimmed milk, coffee, tea and cocoa.

The fluid allowed is restricted to the quantity present in the food, plus that which is necessary for the comfort of the individual patient, amounting usually to 1200 to 1500 cc. The amount of salt allowed is the quantity sufficient to make the food palatable.

I might state at this point that the use of pure proteins in the feeding of cases of chronic nephrosis is at present under investigation.

Disappearance of the edema and even marked diminution of the albuminuria does not mean a complete cure of the nephrosis. A complete cure is established when, besides the disappearance of symptoms, there is also a normal state of the blood as regards the cholesterol, protein and the albumin-globulin ratio.

In conformity with the view that chronic nephrosis is a metabolic disease related to a state of hypothyroidism, I have used thyroid gland therapy in a number of cases which were more obstinate, and I had gratifying results. The relationship of the thyroid gland to obscure cases of edema has been made the subject of a study by Eppinger.[65] In his work he presents most remarkable data of increased diuresis following administration of the thyroid gland in various forms of edema. No basal metabolism studies, however, are given. Volhard[66] has also seen good results from thyroid gland administration.

The effect of thyroid feeding upon some cases of nephrosis is so striking that there can be but little doubt as to the relation of thyroid deficiency to this disease. The frequent occurrence of nephrosis in children and the usual gravity of the condition in such cases suggest the possibility of its being due to a deficiency of some factor in the food—possibly a vitamine.

In this connection the experience of writers on war nephritis is of interest who found a peculiar tendency in the kidneys to fatty degenerative changes, and who ascribe these changes to disorders of nutrition (Munk).[67] This possibility should be borne in mind in future studies of the subject.

THE PREVALENCE OF FREE HYDROCHLORIC ACID IN CASES OF CARCINOMA OF THE STOMACH.

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Achlorhydria is so frequently associated with carcinoma of the stomach that one acquires the habit of looking for it as a diagnostic

[65] Zur Pathologie und Therapie des menschlichen Odems, Berlin, 1917.
[66] Loc. cit.
[67] Loc. cit.

sign of carcinoma. This habit grows until one hesitates to make a diagnosis of carcinoma of the stomach in the presence of any appreciable amount of free hydrochloric acid in the gastric secretions. Clinicians who have the opportunity to observe the results of fractional analysis of the gastric contents find that achlorhydria is not essential to the diagnosis of gastric carcinoma. As a means of corroborating this finding a statistical review was undertaken of the analysis of gastric contents in cases in which operation was performed for cancer at the Mayo Clinic during the years 1918, 1919, and 1920. Since the results for each year were quite uniform the data were studied as a whole. When the surgeon noted the location of the lesion in the pyloric, middle, or cardiac portion of the stomach this was considered in classifying the data.

During the three years, there were 551 patients with gastric carcinoma and 80 patients with carcinomatous ulcer operated on. Of the latter, with one exception, a case of gall-stone, gastric lesions were clinically suspected. Forty-five per cent of the cases were diagnosed ulcer, 41.25 per cent cancer, and in 12.15 per cent the diagnosis was suspected gastric malignancy.

The gastric acidity was first classified separately according to the location of the lesion and then together. Of the 551 patients with carcinoma, 47 did not have test meals because they were too weak to stand them, because the stomach was found empty on aspiration, because of a mistaken diagnosis, because the patient's condition demanded an emergency operation and so forth. In 122 patients the lesions were not located by the surgeon, although resection was performed. In 66 patients the condition was found inoperable. An exploration or a gastro-enterostomy only was made for the relief of an obstruction. In 297 patients the lesions were in the pyloric end of the stomach, in 27 in the middle portion, and in 39 in the cardiac end. These data were taken from patients who were operated on; this accounts for the preponderance of pyloric lesions which are favorable for surgical measures, whereas lesions higher up are not accepted by the surgeon (Table I).

TABLE I.—CARCINOMA.

	Cases.	Per cent.	Achylorhydria.	Per cent.	Hypoacidity.	Per cent.	Normal.	Per cent.	Hyperacidity.	Per cent.	No test meal.	Per cent.
Not located	122	22.14	67	54.9	12	9.83	22	18.+	4	3.27	17	13.9
Inoperable	66	11.97	40	60.6	8	12.12	11	16.66	4	6.06	3	4.54
Pyloric	297	53.9	154	51.85	53	17.84	54	18.18	15	5.05	21	7.07
Middle	27	4.9	11	40.74	11	40.74	5	18.51	0	....	0	
Cardia	39	7.07	24	61.54	3	7.69	4	10.25	2	5.12	6	15.38
Ignoring location.	551	.....	296	53.72	87	15.78	96	17.42	25	4.53	47	8.53

The normal amount of free hydrochloric acid was estimated at from 20 to 40. The classification of the lesions according to location revealed little of importance. However, in 51.85 per cent of the pyloric lesions achlorhydria was present and the pyloric end of the stomach is not supposed to possess any acid-forming cells that could be destroyed by a new growth. In 5.05 per cent of the pyloric lesions the values were hyperacid. In the cardiac portion, the location of the acid-forming cells, the achlorhydria was 61.54 per cent and the hyperacid values 5.12 per cent.

The location of the lesion apparently does not materially influence the degree of the acidity. It is impossible from these statistics to determine the percentage of occurrence of any one degree of acidity in any one division of the stomach. Pyloric lesions predominate in patients operated on and therefore they have the highest percentage occurrence in any one degree of acidity.

Attention is called to the total findings in Table I, in which the gastric analyses have been studied without reference to the location of the lesion. Only 53.72 per cent., about one-half of the patients, had achlorhydria; 15.78 per cent had free hydrochloric acid in small amounts. In 17.42 per cent the gastric acidity was normal and 4.58 had hyperacid values. The sum of the last two figures show that 21.95 per cent, or more than 1 case out of 5, had normal or hyperacid values. Thirty-seven and seventy-eight hundredths per cent, or about 2 out of 5 cases, had a certain amount of free hydrochloric acid. The occasional marked difference between free and total acidity is shown in Table II; this occurs particularly in pyloric lesions. It cannot be explained by obstruction with retention of the neutralizing food, because in the cases in which the difference in the acidity was more than 40 there was obstruction only in 34.28 per cent.

In Table III are data concerning gastric ulcer undergoing malignant change. Only 22.5 per cent of cases had hypoacid values. The sum of the percentages of those having some acid (hypoacidity, normal acidity and hyperacidity) is 72.5. The extent of the malignancy therefore seems to influence the amount of free acid because the same total in carcinoma cases was only 37.78 per cent. In Table IV it may be seen that out of 631 cases of gastric carcinoma in all stages of development 49.76 per cent showed achlorhydria; 15.2 per cent hypoacidity, 19.96 per cent normal acidity and 6.97 per cent hyperacidity. The sum of the last two figures shows that 26.93 per cent, or about 1 case out of 4, had normal or hyperacid values. Forty-two and fourteen hundredths per cent had some free hydrochloric acid present. One should expect then to find free hydrochloric acid in about every other case.

It is seen, therefore, that achlorhydria is present in a little less than one-half of the cases of carcinoma of the stomach. Normal or hyperacid values can be expected in more than one-fourth. The

TABLE II.

Achlorhydria.				Hypoacidity.				Normal.				Hyperacidity.				No test meal.				Not located.				
Pyloric.	Middle.	Cardiac.	Inoperable.	Pyloric	Middle.	Cardiac.	Inoperable.	Pyloric.	Middle.	Cardiac.	Inoperable.	Pyloric.	Middle.	Cardiac.	Inoperable.	Pyloric.	Middle.	Cardiac.	Inoperable.	Achlorhydria.	Hypoacidity.	Normal.	Hyperacidity.	No test meal.
24–0	20–0	8–0	16–0	32–15	28–16	28–16	32–16	46–26	40–20	42–30	46–26	76–56		60–42	76–60	323060		338252		20–0	26–10	40–28	60–40	301646
12–0	20–0	10–0	8–0	30–18	24–6		24–14	42–32	44–20	34–22	54–36	66–44			80–56					8–0	28–16	46–24		332781
8–0	0–0	10–0	12–0	20–10	26–16		24–14	34–24	40–20		44–30	90–62			94–50	337719				10–10		40–20		304330
12–0	20–0	12–0	10–0	20–6	30–16		30–10	54–34			30–20	64–44			66–40	326764				12–6		50–24		302254
14–0	10–0	10–0	12–0	16–6			28–10	40–20			40–26	56 44								20–0				332312
12–0	14–0	10–0	10–0	36–16				48–28			42–20	60–40								12–0				338465
10–0		12–0	16–0	38–16				50–30				76–40								12–0				
12–0		10–0	12–0	34–10				58–38				78–44								14–0				
14–0			10–0	40–18				38–22				60–44												
10–0			26–0	32–16				38–20				64–44												
20–0			20–0	36–16				50–24				62–40												
20–0			12–0	38–18				48–28																
20–0			20–0	52–8				44–24																
12–0			16–0	22–8				54–34																
10–0			20–0	40–10				64–38																
16–0			50–0	38–18				78–32																
14–0			10–0	28–12				56–38																
30–0			10–0	28–8				46–24																
12–0			10–0	28–12				56–38																
30–0				75–12				60–34																
32–0				26–12				66–30																
48–0				34–14				44–24																
8–0				30–14				44–24																
12–0				12–2				76–34																
20–0				24–18				56–34																
20–0				58–18				40–28																
50–0				58–18																				
18–0				60–16																				
10–0				36–16																				
12–0				30–16																				
10–0				84–14																				
14–0																								
10–0																								
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34–0																								
20–0																								
18–0																								
30–0																								
20–0																								

Acidity is expressed in the number of cubic centimeters of decinormal sodium hydroxide necessary to neutralize 100 cc of gastric juices.

FREE HYDROCHLORID ACID.

Achlorhydria	0	Normal acidity	20–40
Hypoacidity	0–20	Hyperacidity	40–+

TABLE III.—CARCINOMATOUS ULCERS.

	Cases.	Per cent.	Achlorhydria.	Per cent.	Hypoacidity.	Per cent.	Normal.	Per cent.	Hyperacidity.	Per cent.	No test meal.	Per cent.
Not located	22	27.50	6	27.27	3	13.63	5	22.72	7	31.36	1	4.54
Inoperable	..	.....	..	.....	..	.....	..	.....	..	.....	..	
Pyloric .	50	62.5	10	20.00	..	12.00	22	44.00	12	24.00	..	
Middle .	3	3.75	1	33.33	..	.....	2	66.66	..	.....	..	
Cardia .	5	6.25	1	20.00	..	.....	1	20.00	..	.....	3	60.00
Ignoring location	80	.....	18	22.50	9	11.25	30	37.5	19	23.75	4	5.00

TABLE IV.—CARCINOMA AND CARCINOMATOUS ULCERS.

	Cases.	Per cent.	Achlorhydria.	Per cent.	Hypoacidity.	Per cent.	Normal.	Per cent.	Hyperacidity.	Per cent.	No test meal.	Per cent.
Not located	144	22.82	73	50.69	15	10.41	27	18.75	11	7.63	18	12.5
Inoperable	66	10.45	40	60.6	8	12.12	11	16.66	4	6.06	3	4.54
Pyloric .	347	54.99	164	47.26	59	17.0	76	21.9	27	7.78	21	6.05
Middle .	30	4.75	12	40.0	11	36.66	7	23.33	..	.....	..	
Cardia .	44	6.97	25	56.81	3	6.81	5	11.36	2	4.5	9	20.45
Ignoring location	631	.....	314	49.76	96	15.21	126	19.96	44	6.97	51	8.08

acid values represent the highest reading obtained by a fractional analysis of the gastric contents; this, I believe, gives a greater chance of obtaining higher and more accurate values than the single tubing.

THE RELATION OF ACROMEGALY TO THYROID DISEASE: WITH A STATISTICAL STUDY.*

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and

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The view that acromegaly is caused by hyperactivity of the anterior pituitary body after epiphyseal union has taken place is

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generally accepted. Cushing,[1] however, adduced experimental evidence to show that the disease is due to some perversion of secretion rather than merely to an excess of normal secretion.

With the slow and gradual development of the affection the sella turcica dilates into a cavity of variable size, as shown by a roentgen-ray examination. In practically all cases of acromegaly that have come to autopsy enlargement or disease of the hypophysis has been found, with a corresponding dilatation of the sella turcica and persistence of the thymus in most instances. The new growths of the pituitary gland may be of different character, *e. g.*, adenoma, sarcoma, carcinoma and cystic degeneration. It is generally held that the majority are adenomata. Sternberg[2] states that the acute form of acromegaly is due to a rapidly progressive tumor, frequently sarcoma, of the hypophysis. The enlargement may be due to functional hypertrophy with or without hyperplasia of the chromophile cells.

On the other hand it has been shown that destructive lesions of this gland may be at times unaccompanied by clinical symptoms of acromegaly.[3] In 1891 one of us (Anders) and Henry W. Cattell reported to the Philadelphia Neurological Society a hemorrhagic tumor of the pituitary body and infundibulum which had been unattended with any signs of acromegaly during life.

Conversely, Arnold and Ponfick[4] have reported cases of acromegaly with the pituitary glands normal in all respects. It is true, as pointed out by Friedman,[5] that all ductless-gland disturbances may manifest themselves clinically without gross or microscopical changes. Hemmeter[6] has also emphasized the occurrence of endocrine syndromes without actual pathological alterations. These are termed "ductless-gland neuroses." Among predisposing factors in acromegaly, the role of some of which are still in doubt, are race, age, sex, heredity and trauma, to which detailed reference will be made hereafter.

In 1886 Rogowitsch,[7] and later Stieda[8] and Hofmeister,[9] noted hypertrophy of the pituitary after removal of the thyroid in rabbits. Bourneville and Bricon[10] state that in sporadic cretinism in which the thyroid is lost the pituitary has been found to be enlarged. Boyce and Beadles[11] and other observers found an increase in size

[1] The Pituitary Body and its Disorders, p. 10.
[2] Nothnagel's Handbook, 1897, p. 7.
[3] Jokoloff: Virchow's Archives, vol. **13.**
[4] Quoted by Cushing: Loc. cit., p. 20.
[5] New York Med. Jour., 1921, **113,** 370.
[6] Ibid., 1914, **99,** 101.
[7] Modern Medicine (Osler and McCrae), 1915, **4,** 803.
[8] Ueber das Verhalten der Hypophysis des Kanninchens nach Entfernung der Schildrüse, Ziegler's Beiträge, vol. **10.**
[9] Fortschr. d. Med., 1892, No. 4.
[10] Arch. d. Neurol., 1886.
[11] Bacteriol. and Pathol., 1892, **1,** 223 and 359; February, 1893. Pathologic Reports, University College, London, 1892–93, vol. **1.**

of the pituitary gland in hyperthyroidism, while Abram[12] noted changes in this gland in a case of carcinoma of the thyroid. Marie and Marinesco[13] described a case of acromegaly in which there was simple hypertrophy of the thyroid and thyroid-like tissue of the hypophysis. Schöneman[14] in 85 cases of goiter found marked changes in the pituitary in all but one instance.

Conversely, in animals subject to experimental hypophysectomy, definite histological alterations in the thyroid have been observed. For example, Caselli[15] found hypertrophy of the entire thyroid apparatus. The view of Comte[16] and Hoskins[17] that these two glands can function vicariously for one another is supported by the results of total or nearly total extirpation of the hypophysis and those of thyroidectomy.

Of 15 cases of pituitary disease in Cushing's series, in which the thyroid was examined microscopically, all showed "a low epithelium with excess of colloid." It should be noted that at the time of his examinations all of the cases were evidencing signs of glandular insufficiency.

Exner[18] relates that in 2 of Hochenegg's cases of acromegaly, after partial extirpation of the pituitary, enlargement of the thyroid occurred. Says Cushing,[19] "It is my impression that the gland is most liable to show enlargement in individuals with clinical evidences of past hyperpituitarism"—suggesting, in other words, that the same underlying biochemical factor causes a hyperplasia of both structures rather than that the thyroid assumes a compensatory and vicarious role for the hypophysis. Observations upon tumors of the hypophysis were described as early as 1810, when Wenzel[20] tried to link epilepsy with diseases of the pituitary. To Friedreich[21] we owe the first attempt to formulate the symptoms of pituitary new growths.

Cushing[22] has described cases of acromegaly in which with overgrowth and overactivity of the anterior lobe are associated symptoms of posterior lobe insufficiency, *i. e.*, adiposis, increased sugar tolerance, polyuria, polydipsia, subnormal temperature, dry skin, loss of hair, epileptiform disturbances and the like.

Pineles[23] has emphasized the clinical relationship between acro-

[12] Liverpool Med.-Chir. Jour., July, 1896.
[13] Anatomie pathologique de l'Acromegalie, Arch. d. méd. exp., 1891.
[14] Virchow's Archives, 1892.
[15] Riv. sper. di fren., 1900, p. 468.
[16] Beitr. z. path. Anat. u. z. allg. Path., 1898, **23**, 90.
[17] Am. Jour. Med. Sci., 1911, **141**, 374, 535.
[18] Beiträge zur Pathologie und Pathogenese der Akromegalie, Mitt a. d. Grenzgeb. d. Med. u. Chir., 1909, **20**, 620–644.
[19] Loc. cit., pp. 280–281.
[20] Ueber den Hirnanhang fallsuchtiger personen, Mainz, 1810.
[21] Beiträge zur Lehre von den Geschwülsten innerhalb der Schädelhöhle, Wurzburg, 1853.
[22] Am. Jour. Med. Sci., March, 1913, p. 313.
[23] Volkmann's klin. Vortr., 1899, p. 242.

megaly and myxedema, as shown, he believes, by the comparatively frequent coexistence of the two conditions, by the similarity of many of the symptoms and by the occurrence of similar pathological changes in the two conditions. Without doubt these two glands exhibit points of resemblance both from a histological and a physiological viewpoint, so that their commonly observed clinical association should be expected. To show the similarity of their effects upon metabolism it is only necessary to call attention to the fact that myxedema occurring before the growth of the bones is completed causes an arrest of ossification. Functional associations between the pituitary, adrenal, thymus, pineal and genital glands are also recognized, but these will not receive consideration here for want of space.

Whether in the cases of associated changes in the pituitary and thyroid the latter shows atrophy or hypertrophy in the majority of the cases is, perhaps, no longer a moot question (*vide infra*). For example, Schönemann[24] believes that an increase of hypophysis may take place in cases of hypertrophy of the thyroid gland; he has, however, "failed to find any compensatory increase of the hypophysis in goiter—that is, in cases of degeneration of the thyroid or in cachexia strumipriva." On the other hand, Souza-Leite,[25] based on an extensive collection of cases, holds that an atrophy of the thyroid is more frequently associated with an enlarged hypophysis than hypertrophy of the thyroid. Hutchinson[26] affirms that the thyroid is atrophied in about 10 per cent of all cases of acromegaly and enlarged in 30 per cent, the enlargement being due usually to cystic degeneration.

It would appear that practically all of the larger earlier post-mortem reports of fatal myxedema in which the hypophysis was examined no abnormalities were observed. We venture to believe, however, that solitary instances of the association of lesions under discussion is decidedly more common than was formerly supposed. Moderate increase in size and microscopical structural changes which are not infrequently present are easily overlooked unless the examinations be thorough and complete.

The effects of hyperactivity of the anterior hypophysis differs in different cases with alterations in the functions of the other internal glands, more particularly the thyroid gland. In this connection the observation of Berkeley[27] that the anterior lobe of the hypophysis is abundantly supplied with sympathetic fibers while the posterior lobe is devoid of such fibers, goes far toward explaining the interrelation between diseases of the former and hyper- and hypothyroidism.

[24] Quoted by Boyce and Beadles: Loc. cit.
[25] L'Acromegalie, Paris, 1890.
[26] New York Med. Jour., 1898, No. 11, vol. **67.**
[27] Quoted by Bell, p. 32.

In a previous paper by us[28] the purpose was, among other things, to collect all cases of pituitary disease recorded in literature covering a period of five years terminating December 31, 1913, and to aid in clearing the question of the relation of hypo- and hyperthyroidism to acromegaly on the one hand and glycosuria on the other. In 5 out of 16 cases (31.5 per cent) of acromegaly in which the thyroid was reported on changes were noted. Of these the thyroid was small in 1, normal in 1, sclerotic and cystic in 1, not palpable in 1, while the remaining case (our own) showed well-marked evidences of hyperthyroidism. These figures would appear to show that the role played by hyperthyroidism in cases of acromegaly is trivial and uncertain. On the other hand they indicate that hypothyroidism is more commonly found in association with pituitary disease.

It is of much interest to note that while acromegaly is regarded as being a rare disease, six years after Marie[29] first described the condition Collins[30] was able to collect about 90 cases from the literature. In 1898 Hinsdale[31] found reports of 130 cases, of which 23 showed exophthalmos, and in the same year Woods Hutchinson collected 218 cases.

In 1893 James J. Putman[32] treated a case of acromegaly with thyroid powder (gr. xv every second day); the condition improved markedly, the enlargement of the hands and feet having practically disappeared. We believe it is safe to infer that in this instance hypothyroidism was associated and that the hypertrophy affected principally the soft tissues. Putman refers briefly to 2 additional cases, "The one stands nearer to acromegaly and the other to myxedema, though in both the diagnosis is doubtful." Both were given thyroids with excellent results. In the former there was a large swelling of the neck, "probably a thyroid, which is diminishing under thyroid extract." There can be but little doubt that this was an instance of combined pituitary and thyroid disease, since hypothyroidism is known to occur in subjects showing enlargement of the gland. Such cases we believe are common examples of advancing hypopituitarism associated with hypothyroidism. They are, as a rule, greatly benefited by careful glandular therapy.

On the other hand Burns's, Benson's and Mosse's cases (quoted by Hinsdale) treated with thyroid extract showed improvement principally in the subjective symptoms, more particularly in the nervous phenomena, without diminution in the size of either the lips, hands or feet. In such an absolute diagnosis of an associated hypothyroidism would be unwarranted. In this connection it is to be borne in mind that in myxedema the hypertrophy affects the

[28] Am. Jour. Med. Sci., 1914, **147**, 323.
[29] Revue de Méd., 1886.
[30] Jour. Ment. Nerv. and Dis., 1892.
[31] Acromegaly, 1898, p. 23.
[32] Tr. Assn. Am. Phys., 1893, **8**, 338.

soft tissues exclusively, although the basal metabolism, especially as related to the nervous system, is decreased in this disease. Improvement in the mental condition, however, in the absence of a favorable effect upon the soft tissues in myxedema is contrary to universal experience

The growing tendency to regard individual cases of glandular disease as being of pluriglandular origin is unjustified. As pointed out by Falta[33] in speaking of pathological correlation, "The disease that has first involved one gland involves in its further course other members of the ductless glandular system." True it is that upon close analysis of the history, symptoms and course of a given case it is quite frequently possible to discern which ductless gland was first affected.

Secondary to primary involvement of the hypophysis the symptomatic indications of both hypo- and hyperactivity of the thyroid may arise. That the converse may obtain, however, seems to be supported by ample evidence, *e. g.*, in certain cases of Graves's disease. Bell[34] has studied the pituitary in disease of the thyroid. He described the results of a histological examination in a case of cretinism in a female who died at the age of thirty-three years; the structural characteristics found indicated considerable activity, which he thinks were probably compensatory in character.

In exophthalmic goiter many more basophils than is normal are found in the pars anterior, while in the pars posterior the number is normal. Certain it is, however, that reliable deductions must await further information concerning secondary pluriglandular effects. At all events it would seem to us highly probable that the effect upon the pituitary (anterior lobe and intermedia) is more marked after the removal of the thyroid than after the removal of other hormonopoietic organs.

Friedman[35] claims there is a certain degree of hypophyseal hyperactivity in hyperthyroid and of hypoactivity of the pituitary in hypothyroid states. If this be true, then, pituitary products are contraindicated in the treatment of Graves's disease, but indicated in addition to thyroid in myxedematous subjects. This dictum receives confirmation from the histological studies of the hypophysis in hyperthyroidism and myxedema by Fry,[36] who points out that in the former condition the histology corresponds to a gland of high activity and in the latter to a gland of low activity. The pituitary in myxedema is anatomically a hypertrophied gland, but physiologically an atrophied one.

It is especially in these hybrids that mild forms of hypothyroidism, which are so difficult to diagnosticate, are liable to occur; but

[33] The Ductless Glandular Diseases, second edition, p. 440.
[34] The Pituitary, William Wood & Co., New York, p. 262.
[35] Loc. cit.
[36] Quart. Jour. Med., 1914–15, **3**, 277.

their recognition is important, as shown by the happy effects of metabolic stimulation by means of thyroid extract so far as the myxedematous manifestations are concerned. As elsewhere stated by one of us:[37] "In both the skin is dry; the subcutaneous fibrous connective tissue is thickened by overgrowth; the tongue is enlarged; the mucous membranes, especially of the nose, soft palate and uvula, are thickened; and menstrual disorders in the female; in both there is irritability of temper, slowness of the mental processes and thick, difficult speech."

Certain obvious features, however, belong to each of these diseases alone when found to be combined. For example, the general bony enlargement with separation of the condyles, spreading apart of the teeth, increased growth of the hair on the head, enlarged joints, the severe headaches and increased muscular strength followed by muscular weakness; in women hairiness assuming the male type, disturbances of vision and bilateral hemianopsia are dependent on the acromegaly; while the tendency to chilling, a subnormal temperature, diminished metabolism, elastic skin—dry and scaly (no pittings)—miniature thyroid, malar flushes, loss of hair, slow small pulse, often arteriosclerosis and slight albuminuria, as well as a peculiarly distorted physiognomy (masked facies), belong to myxedema. Attention should be directed here to those minor forms in which the symptoms are merely suggestive of associated hypothyroidism. In such the cautious use of thyroxin is advised in order to confirm the diagnosis.

In associated hyperthyroidism the cardinal symptoms, such as tachycardia, tremor, exophthalmos, nervousness, increased sweating and increased metabolism, may be more or less frankly expressed, in which case an assured diagnosis is beyond question. In certain cases the degree of hyperthyroidism is moderate or even slight and the symptoms presented are indefinite and variable. Slight tachycardia, a moist delicate skin, a tendency to diarrhea, often polyuria, amenorrhea, slight increase in size of the thyroid, and somewhat widened palpebral fissures and an increased metabolic rate, which is a reliable criterion, are among the most significant diagnostic features in these mild, atypical forms. In the sympathicotonic type one may observe exophthalmos with tachycardia, but no sweats or diarrhea, marked falling out of the hair or alimentary glycosuria.

In this connection Janney's[38] view that the classic symptoms of exophthalmic goiter are of toxic origin or due to a perverted rather than to mere excess of thyroid secretion is to be recollected. If we accept this theory we shall be in a position to appreciate how toxic and hypothyroid symptoms may be combined in a given case. Again, in cases of acromegaly with associated exophthalmic goiter

[37] Anders: Diagnosis of Myxedema, Am Jour. Med. Sci., 1920, **160**, 801.
[38] Arch. Int. Med., August, 1918, p. 187.

and deficiency symptoms small doses of thyroid extract may prove useful while larger ones would produce an unfavorable effect. Before forming a final diagnostic opinion, however, exophthalmos due to the pressure effects of the hypophyseal enlargement must be eliminated. It is to be recollected that a state of thyroid insufficiency following hypophyseal overactivity is not reached before death in all cases, but only in those in which degenerative changes occur.

An examination of the literature reveals not a few cases of combined pituitary and thyroid disease in which the manifestations of hypothyroidism overshadow those of hypophyseal disease. To overlook the true nature of these is unfortunate in view of the happy effects of appropriate glandular therapy. We have personally observed modifications of the function of the thyroid in two cases of acromegaly, which are here briefly detailed:

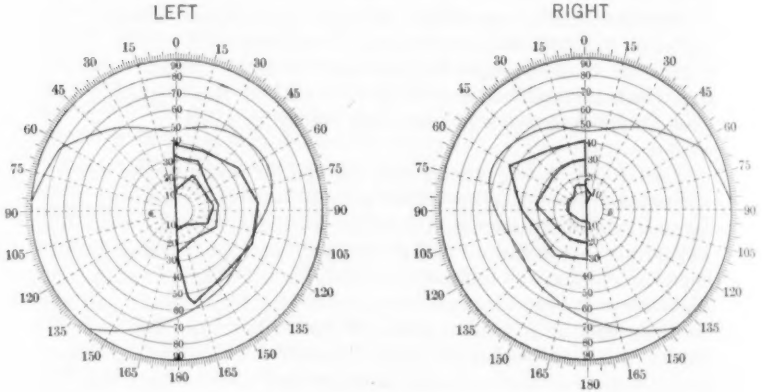
Case I.—A. J. M., female, aged thirty-four years; single; weight, 168 pounds; teacher in the public schools; was referred to one of us for study and treatment by Dr. S. Lewis Ziegler, November 3, 1917. The paternal grandfather died of apoplexy, also the maternal grandfather. The patient had some of the childish diseases and during adolescence repeated attacks of tonsillitis. Eight years ago she was operated on for tuberculosis of the "right tube and ovary"; the wound is still unhealed (fecal fistula). The patient had been taking little exercise and menstruation had always been delayed and scanty, followed by amenorrhea during the past fourteen years. For a long time she had been constipated and complained of nervousness, irritability and was annoyed by any noise; during the past year she had much headache and always felt chilly. During the past two years she noticed a divergence of the left eye, and states that for about eight years she had large bones.

Status Praesens. Bones of face, hands and feet as well as those of the trunk unusually large; hands and feet especially broad in bony parts, spade-like; lower jaw prognathus. Complains of severe headaches at times with nervousness and marked irritability of temper; speech is slow, thick and leathery.

Myxedematous infiltration of the skin of the face and extremities is present, but had not been previously recognized. An associated symptomatic anemia is more marked than usual. For example a blood count showed erythrocytes, 3,110,000; leukocytes, 6000; color index, .9; hemoglobin, 55 per cent. The skin exhibits a slightly yellowish hue with marked pallor of the mucous membranes. The thorax is negative; a fecal fistula is noted in the right lower quadrant of the abdomen. The thyroid is not palpable. The urine proved negative and there is increased sugar tolerance.

Dr. Ziegler reports eye-findings as follows: "She first noticed diplopia about one year ago, which doubtless was caused by the

muscular error in her eyes, which amounts to a hyperphoria of 4 degrees and an exophoria varying from P 18 degrees to P 20 degrees. Her refraction is compound hypermetropic astigmatism of low grade. I have corrected the hyperphoria, but cannot correct the exophoria without again causing her diplopia, as one eye wanders off far enough to limit her to monocular vision. The nerve head shows slight pallor on the temporal side. The fields are absolutely hemianopic with some contraction, as is indicated in the charts of the same, which I enclose."



A roentgen-ray study by Dr. G. E. Pfahler follows: "I find great thickening of the skull. The cranial vault is approximately 2 cm. in thickness—three or four times as thick as normal. There is a tumor in the region of the pituitary and this tumor has extended both upward above the sella and has broken through the floor of the sella, extending into the region of the sphenoid. This is the first time that I have seen such a condition (in which the tumor has extended through the floor). The clinoid processes are not widely separated or destroyed, as is commonly the case, probably due to the fact that the tumor has extended downward more than upward. The hands show the thickening about the ends of the distal phalanges, and in fact general thickening about the ends of all of the phalanges and of all of the metacarpals. They have the appearance that we commonly find in acromegaly." The case is looked upon as one of acromegaly with associated myxedema and tuberculosis.

The use of thyroid extract in small doses has been remarkably effective for good. Not only has there been a marked subsidence of all of the myxedematous features, but the headaches, speech and nervous irritability have also been greatly relieved. The bony skeleton, however, has remained stationary.

CASE II.—A. H., aged forty-six years, female, occupation cook, weight 170 pounds, height 5 feet 9½ inches, first came under the care of our surgical colleague, Dr. William L. Rodman, in the Medico-Chirurgical Hospital, December 5, 1913, at which time she was suffering from a gangrenous wound, inflicted by a fish-bone, of the left hand. A few days later the patient was referred to the medical service (to us) for study and treatment. Polydipsia, polyuria and glycosuria, as well as bulimia, were all prominent features throughout the illness. The percentage of sugar at first was 5 per cent, but at the end of one week it rose gradually to 7 per cent, and remained at this level until the end.

The typical symptoms of acromegaly were in evidence. According to the history the bones of the hands and face began to enlarge four years ago while the glycosuria set in about two years later. A roentgen-ray examination by Dr. Pfahler showed marked lipping at the edges of the articular surfaces of the metacarpal bones and phalanges, such as is found in acromegaly, and also a tumor of the pituitary gland, with absorption of the clinoid processes. The diagnosis of associated hyperthyroidism was quite apparent from the noticeable enlargement of the thyroid gland, together with tremor, tachycardia and exophthalmos. The indications of exophthalmic goiter were most probably developed after the glycosuria had existed for an indefinite period of time, although being, as is usual, of insidious origin, it was impossible to fix the precise date of onset. The Wassermann reaction gave a negative result.[39]

With a view of indicating the true pathological relationship between disease of the hypophysis and thyroid the results of a statistical study are subjoined. The total number of cases collected by us, which was 215, includes only a few that were reported prior to the publication of the paper of Dr. Hinsdale in 1898 and that of Hutchinson in 1902. Table I is a detailed tabulation of 91 cases in which thyroid disturbance was associated.

It should be pointed out that the notations to be found in the columns headed hyper- and hypothyroidism are the inferences drawn by the original reporters, with few exceptions. Failure to record the sugar tolerance and condition of the thyroid gland and its function in numerous cases is to be regretted. It is interesting to note that all of our series, or 215 cases, occurred in the white race with a single exception, which was reported by Yamada, of Tokio (*vide* Table I). Trauma played a role in 3 cases and in 2 the disease followed "psychic trauma." According to these findings the influence of traumatism as a disposing factor is insignificant. There can be no doubt but that a family type exists, although the influence of heredity must, on the whole, be trivial, as evidenced by our results, namely, two instances only of the entire series.

[39] This case is more fully reported in a previous article by Anders and Jameson, loc. cit.

TABLE I

Reporter.	Reference.	Age.	Sex.	Lesions in thyroid.	Hyperthyroidism.	Hypothyroidism.	Lesions in pituitary.	Glycosuria.	Remarks.
Lancereaux	Semaine méd., 1895, xv, 61	40	F	Hypertrophy	Present	....	....	Present	Trauma.
Henrot	Quoted by Lancereaux, loc. cit.	36	M	Goiter	Present	....	Tumor size of hen's egg	Present	Reported in 1877; heart hypertrophied.
Valat	Idem.	..	..	Goiter	Present	....	....	.....	Reported in 1893.
Haskovec	Wien. klin. Rundschau, 1895, ix, 257	35	M	Atrophy	....	....	....	Absent	Head injury followed by meningitis.
Sears	Boston Med. and Surg. Jour., 1896, cxxxv, 16	45	F	....	....	Present	....	Absent	Improved by thyroid administration.
Dodgson	British Med. Jour., 1896, i, 660	23	F	Enlarged					
Worcester	Boston Med. and Surg. Jour., 1896, cxxxiv, 413	70	F	Not palpable	....	Marked	Sarcoma with psammomatous degeneration	.....	Myxedema disappeared under thyroid treatment.
Furnival	Lancet, London, 1897, ii, 1190	58	M	Slightly enlarged and altered in function	....	....	Adenoma-cystic degeneration		
Dalton	Idem.	..	..	Normal, except thyroid juice unusually fluid	....	Present	Sarcoma or hypertrophy and posterior lobe almost disappeared	Present	Thymus normal.
Murray	Edinburgh Med. Jour., 1897, i, 170	37	F	Goiter	Present	....	....	Present	Pulmonary tuberculosis.
Murray	Idem.	63	F	Large cystic goiter	Absent	....	....	Absent	
Murray	Idem.	34	F	Enlarged	Present	....	Enlarged	Present	Pulmonary tuberculosis; thymus hypertrophied.
Schiff	Wien. klin. Wchnschr., 1897, x, 277	37	M	....	....	Present	....	Increased tolerance	

Schiff	Ztschr. f. klin. Med., 1897, xxxii, 289, Suppl.	..	..	....	....	Present	....	....	Unable to consult article
Osborne	Tr. Assn. Am. Phys., 1897, xii, 262	47	M	Enlarged 101 gm., extrathyroid in chest, 36½ gm.	....	....	Sarcoma (?)	.....	Heart enormous.
Comte	Beitr. z. path. Anat. u. z. allg. Path., 1898, xxiii, 90	46	F	Much enlarged	Present	....	Enlarged 0.415 gm.		
Comte	Idem.	32	F	Enlarged 390 gm.	Present	Absent	Enlarged 0.85 gm.		
Bailey	Philadelphia Med. Jour., 1898, i, 789	65	F	Parenchymatous hypertrophy; nearly 3 times normal weight	....	....	Adenoma		
Hunter	Tr. Path. Soc., London, 1898, xlix, 246	52	M	Hypertrophy	....	....	Hypertrophy		
Neal	Ibid., p. 237	41	F	Parenchymatous goiter 6½ oz.	Absent	....	Hypertrophy	.....	Slight improvement under thyroid.
Coe	Jour. Am. Med. Assn., 1898, xxxi, 1347	68	F	Small	....	....	....	Absent	Homicidal.
Thompson	Med. Press and Circ., London, 1898, n. s., lxv, 377	19	F	....	....	Present	....	Absent	
Ponfick	Ztschr. f. klin. Med., 1899, vol. i.	47	M	Marked atrophy	....	Present	Chronic interstitial inflammation and atrophy		
Lediard	British Med. Jour., 1903, i, 789	43	F	Bilateral goiter (large)	....	....	....	Previous glycosuria	Left lobe removed with improvement in pressure symptoms.
Cattle	Ibid., p. 780	30	F	Goiter	Present	....	....	Absent	Exophthalmos, tachycardia and excessive sweating.
Snell	Ibid., ii, 131	38	F	Not enlarged	....	Present	....	Absent	Improved under thyroid treatment.
Launois and Roy	Nouv. iconog. de la Salpêtrière, Paris, 1903, xvi, 163	36	M	Hypertrophy; 250 gm.	....	....	Large epithelioma	Present	

TABLE I.—(*Continued.*)

Reporter.	Reference.	Age.	Sex.	Lesions in thyroid.	Hyperthyroidism.	Hypothyroidism.	Lesions in pituitary.	Glycosuria.	Remarks.
Heising	Wisconsin Med. Jour., 1903–04, ii, 684	38	F	Small	....	....	....	.....	Preceded by severe psychic trauma; thymus persistent.
Bate	Louisville Month. Jour. Med. and Surg., 1903–04, x, 374	28	F	....	Probable		....	.....	Attributes tachycardia (100) to overaction of thyroid-like tissue in pituitary.
Salomon	Berl. klin. Wchnschr., 1904, xli, 635	49	M	....	Probable	....	....	.....	Increased metabolism; skin resembles myxedema.
Salomon	Idem.	42	M	....	Present	....	....	.....	Increased metabolism; skin resembles myxedema; marked arteriosclerosis.
Greene	New York Med. Jour., October, 1905, p. 846	25	M	Small	....	Present	....	Absent	Myxedema disappeared under treatment.
King	South. California Pract., 1905, xx, 410	37	M	....	Absent	Previous myxedema	....	Absent	
Kerry	Ophth. Rev., London, 1905, xxiv, 193	50	M	....	....	Probable	....	.....	Marked improvement under thyroid treatment.
Ballet and Laignel Lavastine	Nouv. iconog. de la Salpêtrière, Paris, 1905, xviii, 176	70	F	Hyperplasia	....	....	Parenchymatous hypertrophy	.....	Hyperplasia of adrenals
Taylor	W. London Med. Jour., 1905, x, 124	34	F	....	....	Probable	....	.....	Sent as case of myxedema.
Schoenborn	Beitr. z. path. Anat. u. z. allg. Path., 1905, Suppl., vii, 468	65	M	Cystic goiter with interstitial inflammation	....	....	Adenoma size of walnut	Absent	Cardiorenal asthma.
Porter	Ophth. Rec., Chicago, 1906, xv, 267	47	F	Greatly enlarged	Present				

Curren	Maritime Med. News, Halifax, 1907, xix, 98	20	F	"Thickening in region of thyroid"	Present				
Haywood	Homeopathic Eye Jour., 1907, xiii, 48	33	F	....	Present	....	....	.....	Improved by pituitary treatment; atrophy of ovaries and uterus.
Sainton and Rathery	Soc. méd. d. hôp., Paris, 1908, xxv, 647	32	F	Atrophy and sclerosis	....	Present	Malignant tumor	Absent	Thymus persistent.
Renon and Delille	Ibid., p. 973	47	F	....	....	Present	Tumor	Absent	
Kocher	Deutsch. Ztschr. f. Chir., Leipsig, 1909, c, 13	30	F	Small	....	....	Sarcoma	Present	Thymus persistent; operation.
Carmody	Lancet, London, 1909, i, 1599	33	F	Previous goiter	....	....	....	Absent	Skin thick but could be pinched, now abnormally active; no improvement under pituitary treatment.
Exner	Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1909, xx, 620	30	F	Enlarged after operation on pituitary	....	....	Malignant adenoma	Tolerance increased	Tongue, lips, hands and feet smaller after operation.
Exner	Idem.	34	F	Isthmus became size of walnut after operation	....	....	Malignant adenoma	Tolerance increased	
Packard	Am. Med., 1910, n. s., v, 539	36	F	Hypertrophy	....	....	*X*-ray unable to demonstrate tumor		
Grove	Bull. Johns Hopkins Hosp., 1910, xxi, 290	47	F	Colloid goiter	....	Present	Enlarged	Absent	Partial thyroidectomy.
East	Jour. Mental Sci., 1912, lviii, 631	43	F	Enlarged	....	....	....	.....	Mental symptoms.
Cushing	Pituitary Body and its Disorders, Philadelphia, 1912, p. 30	35	M	Small	Absent	Absent	Adenoma	.....	Ac. secondary to gigantism; exophthalmos due to neighborhood pressure.
Cushing	Ibid., p. 36	26	F	Colloid goiter	Absent	Absent	Adenoma		
Cushing	Ibid., p. 85	36	M	Large and colloidal	Absent	Absent	Tumor	.....	Slight acromegaly followed by hypopituitarism; trauma.

TABLE I.—(*Continued.*)

Reporter.	Reference.	Age.	Sex.	Lesions in thyroid.	Hyperthyroidism.	Hypothyroidism.	Lesions in pituitary.	Glycosuria.	Remarks.
Cushing	Ibid., p. 137	40	M	Slightly enlarged	Absent	Absent	Slight enlargement of sella turcica	.....	Hypertrichosis.
Cushing	Ibid., p. 140	38	M	Colloid goiter	Absent	Absent	Chromophil-struma		
Cushing	Ibid., p. 150	59	M	"Plunging goiter"	Former	Absent	Enlarged	.....	Goiter removed.
Cushing	Ibid., p. 154	42	M	"Possibly enlarged"	Absent	Probable	....	.....	Benefited by thyroid treatment; complicated by gigantism, hay fever and tuberculous adenitis.
Cushing	Ibid., p. 194	33	M	Enlarged; excess of colloid	Absent	Absent	"Functional hyperplastic change"	.....	Secondary to hydrocephalus.
Holmes	Proc. Roy. Soc. Med., London, 1912–13, vol. vi, Neurol. Ophth. Sect., X	36	F	....	....	Probable	Sella turcica enlarged	.....	Improved under thyroid treatment.
Garrod	Ibid., lxxviii	..	..	....	....	Present	Sella turcica enlarged	.....	Improved under thyroid.
Brown	Ibid., lxxxvii	40	F	Cystic goiter	....	"Possible myxedema"	....	Tolerance increased	Previous acromegaly, now hypopituitarism; some improvement under thyroid.
Bartlett	Tr. Chicago Path. Soc., 1913, ix, 56	25	M	Colloid goiter	....	....	Chromophil-cell adenoma	.....	Thymus persistent.
Gordinier and Kirk	Albany Med. Ann., 1913, xxxiv, 189	39	F	Distinctly enlarged	....	....	Tumor		
Grinker	Jour. Am. Med. Assn., 1913, lxi, 235	49	M	Absent	....	Present	Large adenoma	Intermittent	Followed infected vaccination and psychic trauma; benefited by thyroid; epilepsy.

Millioni	Riforma med., Naples, 1913, Nos. 39, 40 and 41, vol. xxix	34	F	Small	....	Present	Marked enlargement; probably tumor	Absent	
Fernsides	Proc. Roy. Soc. Med., London, 1913-14, vii; Electro-therap. Sect., 46	40	F	Not palpable	....	Present			
Dunn	Am. Jour. Med. Sci., 1914, cxlviii, 214	61	M	Small	....	....	....	Tolerance increased	Hemoptysis; non-tuberculous; angioneurotic edema.
Anders and Jameson	Ibid., p. 323	46	F	Goiter	Present	....	Tumor	Present	Gangrene.
Osborne	Proc. Connecticut State Med. Soc., 1914, p. 164	40	M	....	....	Present			
Chizet	Lyon méd., 1914, cxxii, 882	15½	M	....	....	Present	Tumor	.....	Polyuria.
Bendell	Albany Med. Ann., 1915, xxxvi, 441	45	F	Colloid enlargement					
Fürth	Med. klin. Berl., 1915, xi, 1347	40	F	Palpation negative	....	Deficient iodine production	Tumor	.....	Temporary improvement under iodide treatment, father had goiter.
Falta	Ductless Glandular Diseases, Philadelphia, 1916, p. 237	32	M	Enlarged	....	....	....	Tolerance increased	Heart enlarged; hypertrichosis.
Falta	Ibid., p. 243	31	M	Slightly enlarged	....	....	....	Tolerance increased	Hypertrichosis.
Falta	Ibid., p. 243	31	M	Not enlarged	Probable	....	Adenoma	.....	Hypertrichosis; thyroid in aggravated symptoms; temporary improvement after operation.
Falta	Ibid., p. 246	33	F	Enlarged	....	....	....	Tolerance decreased	Marked hypertrichosis; lues.
Falta	Ibid., p. 253	37	F	....	Present	....	Grayish-red tumor	Tolerance decreased	
Falta	Ibid., p. 266	31	F	....	Present	Present	....	Tolerance decreased	Hyper-followed by hypothyroidism.

TABLE I.—(*Continued.*)

Reporter.	Reference.	Age.	Sex.	Lesions in thyroid.	Hyperthyroidism.	Hypothyroidism.	Lesions in pituitary.	Glycosuria.	Remarks.
Futcher	Med. Clin. North America, 1917, i, 131	67	F	....	Absent	Possible association of myxedema	Sella turcica enlarged	Tolerance increased	Possible early paralysis agitans.
Soner	Med. Jour. So. Africa, 1918, xiii, 102	34	F	....	Absent	Present	....	.....	Improved under thyroid treatment.
Yamada	Mitt. a. d. Med. Fac. d. k. Univ. z. Tokyo, 1918, viii, 411	17	M	Hypertrophy	....	....	....	.....	Thymus persistent; died of beri-beri.
Good and Ellis	Endocrinology, 1918, ii, 431	58	M	Atrophy	....	Present	Hemangio-endothelioma	Tolerance increased	Thymus persistent; testes and adrenals atrophied and sclerotic.
Lewis	Laryngoscope, 1918, xxviii, 604	34	F	....	....	Present			
Loewenberg	Internat. Clinics, 1918, 28th ser., iii, 154	34	M	Slightly enlarged	....	....	Tumor (calcified)	.....	Pulmonary tuberculosis.
Roth	Berl. klin. Wchnschr., 1918, lv, 305	28	M	Enlarged	....	....	Tumor	Absent	Developed copious milk secretion.
Howard	Am. Jour. Med. Sc., 1919, clviii, 830	31	M	Slight cystic degeneration	....	Probable	Round-cell sarcoma	Tolerance increased	
Howard	Idem.	47	F	Slight goiter	Probable	....	....	Present	
Webster	Arch. Radiol. and Electro., London, 1919–20, xxiv, 261	..	..	Enlarged	....	....	....	Tolerance increased	Headaches relieved by *x*-ray.
Tierney	Med. Clin. North America, 1920, No. 3, iv, 799	40	M	Enlarged	....	....	....	Tolerance increased	Father and sister acromegalic types.
Barr	New York Med. Jour., 1920, cxi, 248	36	M	Enlarged	....	....	Sarcoma	.....	Imbecile.
Bernstein	Not published	39	M	Small	....	Probable	Large adenoma	Tolerance increased	Operation relieved headache, preserved vision; acromegaly stationary since.
Anders and Jameson	Not previously published	34	F	Small	....	Present	Tumor	Tolerance increased	Improved by thyroid treatment.

TABLE II.—TOTAL CASES OF ACROMEGALY, 215

Age (cases mentioned, 195).		Sex (cases mentioned, 194).		Lesions of pituitary (cases mentioned, 99).	Lesions of thyroid (cases mentioned, 68).	Glycosuria (cases mentioned, 91).	
Male.	Female.	Males.	Females.			Present.	Absent.
37.14 Average age, 38.3	38.76	90 (46.4 per cent)	104 (53.6 per cent)	"Tumor" . . . 41 Adenoma . . . 15 Sarcoma . . . . 12 Sella turcica enlarged 13 Enlarged . . . 6 Hypertrophy . . 3 Various 9	Enlarged . . . . 24 Goiter . . . . 20 Atrophy . . . . 17 Hypertrophy . . 7 Functional . . . 23	32 (35.2 per cent)	59 (64.8 per cent)

TABLE III.—COMBINED ACROMEGALY AND THYROID DISTURBANCE, 91 CASES

Age (cases mentioned, 86).		Sex (cases mentioned, 86).		Lesions of pituitary (cases mentioned, 47).	Lesions of thyroid (cases mentioned, 68).	Glycosuria (cases mentioned, 47).	
Male.	Female.	Males.	Females.			Present.	Absent.
39.64 Average age, 39.85	39.98	37 (43 per cent)	49 (57 per cent)	"Tumor" . . . 13 Adenoma . . . 11 Sarcoma . . . . 6 Enlarged . . . . 4 Sella turcica enlarged 4 Hypertrophy . . 3 Various 6	Enlarged . . . . 24 Goiter . . . . 20 Atrophy . . . . 17 Hypertrophy . . 7 Functional . . . 23	14 (30 per cent)	33 (70 per cent)

TABLE IV.—ACROMEGALY WITHOUT THYROID DISTURBANCE, 124 CASES

Age (cases mentioned, 109).		Sex (cases mentioned, 108).		Lesions of pituitary (cases mentioned, 52).		Glycosuria (cases mentioned, 44).	
Male.	Female.	Males.	Females.			Present.	Absent.
35.4	37.67	53 (49 per cent)	55 (51 per cent)	"Tumor" . . . . 28 Sella turcica enlarged . . . 9 Sarcoma . . . . . 6 Adenoma . . . . . 4 Cyst . . . . . 2 Enlarged . . . . . 2 Degeneration 1		18 (41 per cent)	26 (59 per cent)
Average age, 37.18							

A review of Table II shows that in 99 cases out of the 215 cases of acromegaly the lesions of the pituitary are mentioned and that in 68 cases thyroid changes are recorded. It is noteworthy that only three more examples of adenomata than sarcomata are reported among the pituitary lesions, it being currently stated by the older as well as recent writers that the great majority of the new growths of this gland in acromegaly are adenomata. The influence of sex upon the incidence of the disease is shown by a slight preponderance in favor of the female. On the other hand Hinsdale's figures indicate that the disease is more common in the male than in the female sex; for example, he found 73 males and 57 females in his series of 130 cases. The average age here given (thirty-eight and three-tenth years), which represents that of the ages reached at the time the cases were reported, is too high, but the date of onset was so frequently indeterminable from the histories recorded in the literature as to make this course necessary. Table III needs no description.

Table IV shows the age incidence to be slightly higher in the combined pituitary and thyroid cases than in the uncombined acromegalics and also a slightly greater preponderance in the female as compared with the male sex by comparison with acromegaly without associated thyroid lesions. It cannot be stated, however, that these figures afford a basis for the claim often advanced that the thyroid is a true sex gland, as is shown by both Graves's disease and myxedema when they occur independently of the acromegaly. For example, both the latter conditions are six to eight times as frequent in the female as in the male. It will be noted that the proportion of cases of adenoma in Table IV as compared with sarcoma is almost three times greater than in Table III, although the figures are too small on which to base any inferences.

TABLE V.—AGE BY DECADES

	Acromegaly without thyroid disturbance.		Acromegaly with thyroid disturbance.	
Under 20 years	3	Under 20 years	3
21 to 30 "	32	21 to 30 "	7
31 to 40 "	34	31 to 40 "	39
41 to 50 "	17	41 to 50 "	25
51 to 60 "	18	51 to 60 "	4
61 to 70 "	4	61 to 70 "	6
71 to 80 "	1	71 to 80 "	2

An inspection of Table V, which presents the age incidence by decades, will show that for acromegaly with associated thyroid disturbance this is considerably higher than in the cases without involvement of the thyroid—an interesting fact. The explanation is probably to be found in the accepted view that thyroid complaints, myxedema in particular, develop later in life than uncomplicated acromegaly, as a rule. This table indicates clearly that

the great majority of cases of acromegaly with thyroid disturbance arise between the thirtieth and fiftieth years of age, and that both during the decade prior to that period of life and subsequently the cases are far less numerous than in acromegaly without thyroid disturbance. Again, it should be noted that in the cases of acromegaly in which thyroid disturbance is combined the latter usually arises a number of years after the onset of the former, *i. e.*, when the stage of hypopituitarism is reached.

TABLE VI.—THYROID FUNCTION, 52 CASES

Hyperthyroidism, 20 (38.5 per cent.)		Hyperthyroidism, 32 (61.5 per cent.)	
Male	5	Male	12
Female	14	Female	18
Glycosuria.		Glycosuria.	
Present	7	Present	2
Absent or increased tolerance	1	Absent or increased tolerance	16

Table VI exhibits the facts bearing on the relative incidence of hyper- and hypothyroidism and on the carbohydrate tolerance as well as the influence of sex on the thyroid function. It will be seen that in the hyperthyroid group the ratio in favor of the female is about 3 to 1 while in the hypothyroid cases it is 3 to 2. Again, the incidence of hypothyroidism as compared with that of hyperthyroidism is about as 3 to 2. With regard to the question of carbohydrate tolerance in cases of combined acromegaly and disturbed thyroid function Table VI demonstrates that in hyperthyroidism the sugar tolerance was decreased in 7 out of 8 cases—ratio 7 to 1. On the other hand in the cases of associated hypothyroidism sugar was absent or tolerance increased in the ratio of 8 to 1. It should be added that of the 16 cases belonging to the latter group in 7 the increased sugar tolerance was determined by the usual tests.

Summary. Our literary studies have revealed an unexpected frequency of associated disturbance of the thyroid function in cases of acromegaly, or 33 per cent, as shown by Table I. It is highly probable that in many instances of pituitary disease with its usual syndrome the coexistence of thyroid alterations and symptoms resulting therefrom were overlooked, as was true of one of the two cases which was reported by us. Our investigations indicate that hypothyroidism is more commonly associated with acromegaly than hyperthyroidism, and that those combined cases which manifest myxedematous features are decidedly improved as the result of the use of thyroid preparations.

It follows that the recognition of the indications of hypothyroidism in connection with acromegaly is a matter of the utmost importance. In cases of acromegaly in which merely suspicious features of either hypo- or hyperthyroidism exist it is strongly urged that

the metabolic rate be determined. The approved sugar tolerance test should be carried out in all cases of acromegaly with a view of determining the state of both the pituitary and the thyroid function. Nothing of special significance bearing upon the etiological factors of the disease under consideration resulted from our studies, with the possible exception of the facts developed in connection with the age groups by decades (*vide* Table V). Our grateful acknowledgements are made to Dr. Andrew A. Anders for valuable assistance in the literary investigations.

EPILEPTOID OR FAINTING ATTACKS IN HYPOPITUITISM.[1]

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We shall make no attempt to analyze hypophyseal dysfunctions in their relationship to epileptiform seizures. This has been fairly well done by Cushing, Johnston and others. Nor shall we discuss the reverse influence, as that of clinical epilepsy, upon the hypophysis, as in the studies of Munson at Craig Colony, or take time and space to consider the subjects of syncope and fainting in general. Even so simple a clinical observation as that of fainting probably has a very complicated and varied psychical and somatic mechanism. We do wish, however, to call attention to the fact that there is an increasing accumulation of clinical data of apparently idiopathic attacks of fainting without general somatic defect of the viscera. During the past few years several such cases have been referred to me on the suspicion that these individuals were suffering from a larval form of petit mal epilepsy.

We may enumerate briefly some of the salient differences between this special type of syncope and petit mal epilepsy. We must first note, however, that it is commonly stated that individuals who have their first attacks of petit mal are only suffering from a form of fainting dependent upon some dysfunctions of the viscera, a weak heart or indigestion. In other words, both laity and physicians are much more likely to believe that the early attacks of petit mal are but a form of syncope and in consequence of little moment.

As for real differential diagnosis: If there be no obvious or immediate exciting cause such as emotional stress or physical shock the individual attack of loss of consciousness is more likely to be nothing more than a syncopal one. Slow and incomplete loss of consciousness also is in favor of the state being simply that of fainting. While a sensation of faintness is common to both, usually it takes on much more elaborate characters such as are seen in the epigastric aura. This aura has the sensation of a rising of an inde-

[1] Read before the American Psychopathological Association, June, 1921.

scribable numbing, burning or full feeling which reaches to the level of the chin, when consciousness is always lost in true epilepsy. In simple syncope frequently there is a sense of dizziness, palpitation in or about the heart, and, what is even more frequently encountered, a sinking uneasiness about the heart. When, however, there is no premonitory warning the diagnosis may be very confusing; under such circumstances one needs to think of the state as probable epilepsy, for less than a third of all epileptics have a warning of the approach of their convulsive seizures. In all syncope there is usually an absence of after-effects, which on the contrary are almost invariably present in epilepsy, such as malaise, mental hebitude and mental confusion. In epilepsy there is little pulse alteration, while this is common after pure syncopal attacks. In the absence of a sharp and distinct loss of consciousness one may look at the episodes as being purely syncopal. The presence of any degree of convulsive movement—independent, of course, of trembling from sheer weakness—marks the state as almost surely epilepsy as well as any transitory phenomena of automatism, sleep or stupor following the attack. Usually the syncope has so little to do with any phase of true vertigo that the absence of any part of the labyrinthian syndrome usually proves that the latter is playing no role in the state. While the classical types of continued syncopal attacks in dysfunctions of the hypophysis are not so often encountered in any large classical material the atypical instances of the states of fainting are perhaps more frequent. These atypical cases usually present themselves as follows: The general practitioner sees them in the rapidly growing boy or girl in late adolescence. There is a history of insufficient sleep and overindulgence in work, play or social functions. This adolescent has a history of having grown very fast—several inches in height at the puberty period—he is physically too large for his age but, as the eugenic law proves, however, he may be entitled to his extra height by comparing those of the parents; it is his too sudden acquirement of it that is pathological. The boy is soft in muscles, perhaps fatigues easily, may be extra awkward, shy or timid. As not infrequently happens he is rather dull in school-work. The latter defect shows the boy is concrete-minded; is restless and discontented with the school discipline; he wants to evade school duties and prefers an outdoor existence, although he cannot stand continuous outdoor activities without fatigue. Physically the patient also shows labile vasomotor changes; takes cold easily; has cold, dusky hands and feet and unexplainable periods of clammy sweats. Above all, when he gets up suddenly or is required to stand perfectly still he has vague or actual syncopal attacks. The clever physician after noting there is no real organic mischief in the boy's makeup cautions him against too intense physical training, etc., and dismisses the case. Perhaps the physician infers unwisely that the patient's nerves and blood need to be built up and prescribes accordingly. If these drugs

are really potent considerable harm may be done, inasmuch as the youth needs neither more nor richer blood, nor does the nervous system need any stimulation, as the latter is already doing its best to quiet the youth by registering extra fatigue and compelling him to sleep long hours. The physician may wisely follow the main trends of compensation already indicated in the individual patient, that of more moderate but continuous outdoor activity and increased hours of sleep (some patients require twelve to fourteen hours to offset an ordinary day's activity), in which case those milder types never return for treatment. Occasionally, half-fearing the condition is epileptic in type, the physician gives sedatives. For a few days the youth appears better, then he returns, showing increased tendencies to syncopal attacks or he becomes very dull and exhausted. Even small doses of sedatives often produce definite toxic effects. On the patient's return for treatment the physician suspects he has prescribed an overdose of the remedy and either reduces it or takes it away entirely or resorts to additional blood and nerve tonics which seriously complicate the clinical picture. As yet the varied and complicated types of endocrine dysfunctions are so little known and described that the average physician little suspects the varied pictures which ductless gland imbalance may present, and many wait until later, when more pronounced types of the text-book descriptions are evolved. While in a real quandary what to do next the physician begins to sense that his patient has all sorts of things which are on the point of beginning, such as flat-foot, gastroptosis, crooked spine, constipation and skin disorders. Inferring that the youth is on the way to an early dissolution, everyone becomes alarmed. Then ensues a general round of visits to various specialists to do patchwork on the particular anatomical part each may find out of order. One of my patients was visiting six specialists, and his nervous invalidism was much encouraged by his narcissistic concern over these various treatments, which were limited to a half-dozen merely because time did not permit of more.

Many of these slighter grades of hypophyseal dysfunctions cure themselves,[2] or, better, the other ductless glands cure hypophyseal

[2] Apropos of this statement the following case may be cited: A young man, aged twenty-seven years, now under my care for a retarded depression, had grown very rapidly while attending a preparatory school between the ages of fourteen and sixteen years. He had a subnormal temperature (97.5° to 98°) the greater part of the time a low blood-pressure and slow pulse (60). He was "cold all the time," and for the greater part of two years he had syncopal attacks on the slightest physical shock, and finally had attacks quite independent of any apparent cause except when required to stand to be measured for a suit of clothing. These syncopal attacks left him weak and trembling. He was six feet tall at sixteen years. Under the advice of his physical trainer at school he engaged less actively in exercise, lived more in the open and took extra bed rest. No further therapy was followed and he recovered from the condition, the last symptoms to disappear being a moderate degree of flat-foot and a permanent acne. It is interesting to note that instead of being concrete-minded and a poor student, as in many of this class, he was the delight of his tutors and easily won several scholarships.

imbalance by atrophy of the thyroid or excessive functioning of the adrenals, but often they do not do so until they have debauched many of the visceral organs in function or structure, or both. In the severe grades of this disorder something radically wrong is earlier recognized and succor follows more promptly if not less surely.

While in a single case one might preach a whole series of medical lessons of neglect in accurate diagnosis, once the disorder is diagnosed the therapy is not essentially simple—least of all is it to be met upon the basis of glandular therapy. While the latter helps, our method of administration is so crude that we must give the gland with caution. No glandular therapy at all is almost better unless due attention is paid to all the other principles of physio- and psychotherapy. In point of fact there are those who despair of ever finding so beautiful a sinecure of gland feeding for endocrinic dysfunction as thyroid administration in cretinism, and have preferred to assist their patients back to health without such aid. While this view is obviously empiric and not scientific it has much to recommend it. Let us see what is really at fault in our specific problem; First of all there is an enduring low blood-pressure and diminished sympathetic tone in the autonomic system. The viscera drains the blood from the cerebral cortex and syncope develops. Usually the adrenals and thyroids come to the rescue and reëstablish blood-pressure, and vasomotor and sympathetic tone are incompletely resumed to await the next calamitous period. As might be expected, all these individuals are underoxygenized. Their tissue metabolism is slow to build up and they are in a state of chronic organic fatigue requiring an enormous amount of sleep. Every case immediately improves with continuous outdoor living and long hours of sleep, but how are these principles to be made permanent in a changing organism during adolescence when the physical and mental equipment for life is to be met? Fortunately the imbalance is not stubborn of correction nor is the fixation once obtained needful of enduring care and attention. It would seem as though the system once having gained its imbalance fixated upon its normal adaptive routine and thereafter made the individuals aware of over-stepping the rules within healthful limits. The whole organism is trying its best to adjust to a plan of overgrowth for the time being. Different bodily functions seem to make an effort to catch up or compensate for the extra skeletal and muscular spurt. The sympathetic and vasomotor systems soon expand and take up their belated functions. One might term the state a form of irregular structural growth of the body, resulting in a disharmony of functioning on the part of the different systems. Three cases out of many that are fairly illustrative are here given:

CASE I.—A boy, now eighteen years old, came to me at the age of fourteen years with a record of poor schoolwork especially in all abstract studies; he was two years in arrears. He had fainting attacks at infrequent intervals when required to stand perfectly still. One of these occurred while being examined and was accompanied by profuse perspiration. He was nearly six feet in height, had low blood-pressure (92) and slow pulse (64). He possessed a childish type of physique—had soft muscles and a piping voice. His movements were slow and awkward. His development during adolescence followed the father's physical and mental history. He was decidedly lazy, sluggish and indifferent to any form of intensive effort. He fatigued easily and required an enormous amount of sleep (twelve hours). Bed-wetting was a permanent habit, and at the age of fourteen it still occurred once or twice a week. A concrete outdoor training was advised, with continued long hours of sleep and also special tutoring. After six months of such treatment the father reported the boy as physically well, and he is now making up his schoolwork, although by preference he prefers an industrial or business career to a professional one.

CASE II.—A young woman, aged twenty-nine years, who has a fairly normal personal and family history aside from a paternal uncle having a sort of "breakdown" in early life, which, judging from the description, may have been similar to our patient's disorder; he had a very large physique and was considerably over six feet tall. After he left indoor work and engaged in agricultural pursuits he enjoyed comparatively good health. Our patient was born at full term, was the first child, healthy and weighed about ten pounds. She is the largest in the family, although all the siblings, four in number, are large built. When about fourteen years of age she had sudden syncopal attacks which came on without cause except when she was required to stand quite still. Immediately following these attacks there would be loose evacuations from the bowels attended by colicky cramps in the abdomen. Soon after these digestive symptoms there would be a sense of fulness in the head and pressure in the ears. These syncopal attacks came on at the time of rapid growth, but were ascribed to indigestion and soon disappeared. The period developed normally at fourteen years. She attended to all her duties encountered in a small New England town and gained a good school education, being particularly proficient in mathematics. Her emotional life developed normally. She taught school for seven years and liked her work, but, as she said, it pulled her down physically and the summer vacations failed to fully restore her for the beginning work in the fall. She was at last obliged to give up teaching on this account and took up Y. W. C. A. work. However, even this type of indoor work proved too taxing, and the syncopal attacks again appeared but unaccompanied by the diges-

tive symptoms. The present attacks come on without warning. She feels a coldness in the epigastrium and a sense of giddiness, which produces fright if she is alone, and she seeks to go to someone. If this is not possible she walks rapidly about, when the syncopal feeling passes off and she begins to feel tired all over. She believes she might faint if she did not move rapidly, although this apparently has never occurred. The attacks always occur by day, usually when she has been sitting or standing for some time. Her verbatim account of one of these is as follows: "I was feeling quite well when I got up. About nine o'clock I went to class and noticed my right hand was cold, but paid no attention to it. A few hours later I went to interview a teacher and found her busy, so I stepped into a room nearby and sat there alone waiting. Suddenly I experienced this sense of coldness, and I got up and walked toward a girl. I was about to attract her attention when I gained control of myself, although I did not feel natural. I was trembling, which is the usual effect after such a spell. There is never any abdominal sensation or indigestion now as formerly."

Physical examination shows a large physique; she is six feet tall. Her pulse was 60 to 64, blood-pressure, 87. There was a dermographism and rather markedly cyanosed hands. Otherwise the physical examination was negative. In the absence of the voice sign the character makeup and any mental stigma of epilepsy the condition was diagnosed as a pituitary dysfunction in which the muscle and skeletal growth apparently outran a proper nervous and circulatory development. There was a marked tendency to gastroptosis and flat-foot; the muscles were flabby and the bony frame was loosely put together. She was given postpituitary and thyroid, with the injunction that she live an outdoor life with long hours of sleep. Too short a period has elapsed to note the final outcome.

CASE III.—This is the case of a young woman, aged twenty-five years, who is nearly six feet in height, which she attained at an early age and whose description corresponds to the previous history as to low blood-pressure, slow pulse, etc. Her first syncopal attacks occurred during her thirteenth year, and were liable to occur on a sudden change of position, such as rising quickly from a chair or from a reclining position. When called on in school to recite or read from the blackboard on rising quickly a wave of darkness would come over her like a cloud before the eyes. It lasted less than a minute and seemed like a slight obstruction of the vision, accompanied by a pressure across the top of the head. There was no state of exhaustion following. During this time she had grown very rapidly and was chronically constipated. The syncopal attacks gradually disappeared after instituting a hygienic outdoor life in the country. Her tendency to such attacks has been overcome to

the extent that she can now engage in indoor work without mishap, and is now taking a course in nursing.

Hardly any material may be found in the literature bearing directly upon our subject. For instance in Stier's work on *Syncopal Attacks*[3] he believes that the faintings are preceded by psychical states as precipitants—obviously a view illy in accord with our subject, wherein psychical factors play little or no role. Timme's[4] study, however, is more pertinent. His case material largely came under his purview because of extreme fatigability in adolescence and persistent headache. He makes no mention of fainting attacks, but otherwise outlines fairly sharply the physical characteristics of our material. He especially stresses the rapid growth, slow sexual maturity, vagatonia and low blood-pressure. In the final stages of middle life he states that petit mal may occur. His therapeutic suggestions are embraced largely in glandular feeding, and he does not seem concerned about detailing the process of compensation which nature uses in restoring the balance.

Summary. There are a number of rapidly growing adolescents who have relatively benign fainting attacks which at first seemingly simulate larval forms of petit mal epilepsy. They are to be differentiated from this latter condition by the absence of the epileptic character and the general physical and mental stigma of the grave disorder. The syncopal states are but a part of the obscure clinical picture of dispituitarism, in which there appears to be an excessive functioning of the anterior lobes of the pituitary gland. Coincident with the fainting attacks may be low blood-pressure, slow pulse, vasomotor ataxia and a host of defective muscular and skeletal displacements. In the psychical sphere one may encounter not infrequently character delinquencies and slow mental development. The line of corrective treatment is physical plus the administration of specific glandular substance. Mild cases recover of their own accord by gradually restoring the glandular and physical balance, but they can be materially helped by proper direction and rest. Timme states that in many cases of dispituitarism such as outlined in my paper the pituitary gland itself compensates by making some bony erosions and thus enlarges the sella for the proper functioning of this gland, and that this fact can be demonstrated by the roentgen ray. In my own cases the roentgen-ray examinations were uncertain of exact determination of this fact.

From the evidence in this brief paper one gains the fact that even in the large group of essential epilepsies and the psychoneuroses in which endocrine dysfunctions are present one must not charge too surely the dysfunction as a real but only a contributing cause for

[3] Syncopal Attacks, Especially among Children, Deutsch. med. Wchnschr., April 8, 1920.

[4] A New Pluriglandular Compensatory Syndrome, Endocrinology, 1918, **2**, 209.

the nervous disorder, for many other precipitants of the disease are surely in evidence which are much more nearly related to the psychic disorder than the circumstance of an endocrinic disturbance. By assuming this position our special glandular therapy will not be too heavily charged with remissness when its administration solely results in failure. No two disorders existent in the same individual are essentially in the relationship of cause and effect.

THE UREA CONCENTRATION TEST.

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The object of this paper is to compare the merits of the urea concentration test with some of the more common tests for kidney function.

The relation of kidney pathology to hypertension has been an extremely interesting and perplexing problem, especially the degree of renal involvement generally found in cases of hypertension, just how much latitude is allowable to the term 'essential hypertension" and whether or not cases of hypertension exist for any appreciable length of time without some demonstrable abnormality in kidney function. Consequently when the work was started, some sixteen months ago, I had in mind the establishment of a routine method, or methods, of examination which would throw some light on the above stated questions.

The number of cases has been limited and the methods of technic were changed frequently in the beginning, therefore the results obtained from the work have been rather disappointing. However, a preliminary report will be given.

I was especially interested in the article by MacLean and De Wesselow,[1] in which they discuss the effects of "war nephritis." They conclude that patients with defective kidneys are unable, after receiving a large dose of urea, to excrete urine with a very high concentration of urea. Further, that the degree of concentration seems to bear a direct relation to the degree of kidney involvement.

The details of the test are as follows:

The patient urinates and at once takes 15 gm. of urea dissolved in 100 cc of water. One hour after taking the urea the patient voids. Two hours after taking the urea the patient again voids. The percentage of urea is calculated in both specimens. If the percentage

[1] Quart. Jour. Med., July, 1919.

of urea exceeds 2 per cent the kidney may be considered as fairly efficient; if below 2 per cent, some disturbance is present and the lower the concentration the more serious the lesion. Cases with a concentration below 1 per cent are rare, but many cases show a concentration of only 1.5 per cent. Occasionally one encounters a case in which marked diuresis is occasioned by the administration of urea, especially if the patient has been imbibing large quantities of water. These cases, of course, can be controlled, and if care is exercised usually a satisfactory test can be obtained. Generally speaking, the second specimen should not exceed 150 cc.

Before discussing the results which we obtained it might be well to dicuss, in brief, the ratio of the urea content of the urine to that of the blood after the administration of large quantities of urea. There is a fact, or rather hypothesis, which confronts us when kidney function is to be considered—namely, the fact that no direct inference can be drawn as to the total functional capacity of the kidneys by the rate of excretion of urinary constituents: that is, the same kidney under the same conditions may excrete at one time much and at another time little. It naturally follows that attempts to draw quantitive anatomical, or even functional inference, from the amount of any constituents excreted, promise little help.

There are two fundamentally conflicting views which, up to the present time, have furnished a foundation for most of our kidney-function tests. Schlayer emphasizes the essential inconstancy in the rate of work of the kidney, even under normal conditions. Ambard, on the other hand, believes that variations in the rate of excretion of urinary constituents, under any and all conditions, are in reality manifestations of the constancy of kidney action, since they are exactly accounted for by the alterations of the concentration of these constituents in the blood and in the urine and do not result from inconstancy in the rate of work of the kidney itself.

Materials used as test substances should be those not affected by extrarenal influences. It will be remembered that Schlayer did not fully emphasize the fact that chlorides are subject to extrarenal influences and that the estimation of sodium chloride in the urine does not necessarily throw any valuable light on the subject of kidney efficiency, because the amount of chlorides excreted may be influenced by the amount of chlorides and water brought to the kidneys for excretion as well as by any degree of difference in the excretability of renal cells. The ideal test substance, therefore, would be a urinary constituent which is a true end-product, in that it is incapable of chemical alteration within the body and is one whose only path of excretion is through the kidneys. Urea fills these requirements to a considerable degree.

Addis has shown that the ratio between the urea content of the urine and that of the blood, over periods of twenty-four hours, is constant in normal individuals who have the same blood-urea con-

centration, while variations in kidney function arise from difference either in environment or in anatomical structure.

Ratios measured over short periods of time vary widely, even though the blood concentration be the same. Probably this variability is due to short-lived alterations in environment which counterbalance one another over a twenty-four-hour period of time, but not over one- or two-hour intervals.

In the normal individual, on a mixed diet, the blood contains from 12 to 18 mg. of urea per 100 cc. When renal function begins to fail, a point is reached at which it becomes difficult for the kidney to deal with the urea and other waste nitrogenous products, with the result that the concentration of these bodies increases in the blood. With an increase of urea in the blood the diseased kidney, of course, is able to excrete the normal amount of urea, and urea estimations alone may be misleading; thus it not infrequently happens that in a case of advanced Bright's disease we find that the average amount of urea excreted in twenty-four hours is equal to that excreted by a normal individual. It was supposed for a time that by estimating the urea content of the blood we could gain information that would throw much light on kidney function. However, it is not infrequent to find an individual with a high degree of kidney insufficiency carrying a normal blood urea content.

MacLæan thought possibly we could determine whether cases with urea retention could be distinguished from those in which the blood urea was within normal limits by difference in the total amount of urea passed in a given time after a dose of 15 gm. of urea. This method failed entirely to differentiate between those patients in whom the blood urea was known to be above normal and those in whom no such retention existed. It was, however, noticed that the concentration of urea in the urine after the dose, appeared to bear a definite relationship to the severity of the case—that is, patients with urea retention passed relatively large quantities of urine with low urea concentration, while patients without retention passed smaller amounts with higher concentration.

As stated above we have not applied this test to a varied group of cases but purposely have confined our work principally to hypertension, and the results are given below.

I have chosen from the list only ambulatory patients who have a definite hypertension and whose blood-urea nitrogen does not exceed 20 mg. per 100 cc, the reason being that it is not our purpose to discuss, in this connection, cases of advanced Bright's disease.

There are fifteen cases in all. Seven pass more than 400 cc of urine at night. Three have a definite fixation of specific gravity over two-hour periods. Five pass less than 1 per cent sodium chloride in twenty-four hours. None has over 20 mg. urea nitrogen per 100 cc of blood. Seven excrete less than 50 per cent phenolsulphonephthalein in two hours. Three concentrate 2 per cent or more urea in the urine following a dose of 15 gm. of urea.

No.	Age.	B. P.	Urine.	Mosenthal.	NaCl, per cent.	BUN: Blood urea nitrogen	Phthalein.	Urea concentration test		
1	60	180–110	1.010–L. amb–acid–alb—few H. casts–480 NU	1.006–1.008	0.5	20	20–20–40	1.5	1.3	1.3
2	40	170–80	1.025–amb–alk–alb tr. few casts–340 NU	1.020–1.029	0.75	18	60–15–75	4.2	2.3	1.7
3	35	248–135	1.032–amb–acid–alb—Mic—300 NU	1.025–1.032	1.00	15	40–30–70	1.4	1.7	1.9
4	50	170–95	1.021–amb–acid–alb—Mic—400 NU	1.020–1.029	1.00	10	15–10–25	1.12	1.3	1.9
5	45	220–90	1.030–alb—mucus + few H. and FG casts 340 NU	1.012–1.034	1.00	15	25–30–55	2.3	2.15	2.67
6	41	220–130	1.022–acid–alb—Muc—Cyls + 250 NU	1.013–1.029	1.4	20	30–20–50	3.15	3.0	2.15
7	36	250–160	1.010(acid–alb tr. Mucus + Pus + 360 NU	1.010–1.014	0.5	15	5–10–15	1.7	1.27	1.27
8	60	280–180	1.012–L. amb–alb—Mic— 460 NU	1.006–1.014	1.1	15	45–20–65	1.56	1.7	7.9
9	56	210–110	1.022–amb–acid–alb—few G. casts 390 NU	1.022–1.030	1.5	20	20–30–50	1.8	2.1	2.2
10	65	295–175	1.028–amb–acid–alb—few H. casts–450 NU	1.022–1.032	1.2	15	12.5–15–27.5	1.6	1.9	1.9
11	50	210–145	1.028–amb–acid–alb—few H. casts–450 NU	1.018–1.029	0.8	20	10–10–20	2.0	1.6	1.9
12	45	210–140	1.035–amb–acid–alb— few G. casts–Pus + 500 NU	1.030–1.041	1.1	10	30–15–45	1.4	1.3	1.2
13	37	210–100	1.031–amb–acid–alb—Mucus + Pus + 275 NU	1.026–1.032	1.2	15	30–25–55	1.6	1.98	1.2
14	37	180–60	1.018–amb–alb—Mis—Aortic Insuf.–380 NU	1.012–1.035	1.0	10	35–30–65	Wass 4	+ +	+ +
15	60	198–130	1.009–acid–alb—few H. casts–230 NU	1.009–1.011	0.5	65	5– 5–10	4.0 2.0	4.0 1.6	4.5 1.8

In the Mosenthal column, we have given the high and the low extreme in specific gravity.
In the phenolsulphonephthalein, we have given first hour, second hour, and total.
In the urea concentration test, the first figure represents percentage just before urea was given and the two following figures represent the first and second hours.
NU– Night urine.

CASE No. 15 is a bed patient, carrying a high concentration of blood-urea nitrogen, evidently a case of chronic interstitial nephritis. Case No. 14 has a positive Wassermann test and a definite aortic regurgitation. His function tests line up in a normal manner. These cases are given merely for comparison. (See Table.)

At first I was inclined to think that the urea concentration test offered little if any more than Mosenthal's two-hour test for specific gravity, considering as I did that both tests simply indicate examples of a common dysfunction—namely, the inability of chronically damaged kidneys to concentrate solids. But as the work advanced I became more and more convinced that this was not absolutely true. You will notice by the chart that only 3 of the cases had a low fixation of specific gravity and only 3 concentrate 2 per cent or more urea in the urine.

I think that the two-hour test for specific gravity gives us valuable aid in kidney function work, especially in the class of cases under consideration. It is extremely important to note the amount of night urine passed. Normally a kidney should be able to excrete the usual amount of nitrogen and other waste material in a normal amount of water; that is, 1200 to 1500 cc of urine should be passed in twenty-four hours with a specific gravity of 1.016 to 1.022. The night urine should not be more than 400 cc. However, with beginning Bright's disease usually one of the first complaints registered by the diseased kidney is for more water. It is unable to excrete the usual amount of solid material unless that material be diluted. The degree of dilution necessary usually runs hand-in-hand with the amount of kidney damage present.

It is of some importance when making these function tests not to change the routine diet or general living conditions of the patient, because we wish to determine the function of the kidney as it actually exists under the patient's usual mode of living and not what the kidney may be made to do under specific conditions. Therefore these patients were not put on any special diet, aside from our cautioning them not to drink water or other fluids between meals while making the two-hour specific gravity observation and also against drinking large quantities before the urea concentration test was done.

Relative to the solution of the questions referred to above—namely: the degree of renal involvement generally found in cases of hypertension, just how much latitude is allowable to the term "essential hypertension," and whether or not cases of hypertension exist over any appreciable length of time without some demonstrable abnormality in kidney function—I can give no definite answer, but I believe, basing my conclusions upon the Mosenthal two-hour test for specific gravity, the amount of night urine passed, and especially upon the urea-concentration test, that the longer the high blood-pressure exists the more kidney pathology one is

likely to encounter, and that the term "essential hypertension" should be limited to those cases in which every available function test has proved normal.

As to the urea concentration test I believe it possesses some merit. From the above observations, as shown in the table, it would seem tnat in high blood-pressure cases beginning kidney dysfunction may be noted at an earlier date with this test that with the function tests commonly used.

BILIARY TRACT DISEASE: SOME LESSONS LEARNED FROM DUODENOBILIARY DRAINAGE. FUTURE PROBLEMS. CITATION OF CASES.

By B. B. Vincent Lyon, A.B., M.D.,

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and

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(*Continued from January, 1922*)

Comment. This case illustrates biliary migraine in its purest form and the hope of relief which can be offered by this method of treatment. This case also illustrates how conditions of this sort, if unrecognized and untreated, inevitably lead later into the final states of gall-bladder pathology and calculus formation in the presence of a "masked" or unsuspected infection, especially when associated with catarrhal exfoliation. Even at this stage it could be repeatedly demonstrated that she was in the precalculus formation period by the finding of cholesterin crystals thrown out by a bile incapable of holding them in solution. We had in our series 19 cases which can be placed in this group. Only 1 other of these was in the pure form of biliary migraine represented in the case reported above. Seventeen had definite migraine sick headaches, with usually terminal biliary vomiting, but showed, in addition, different disturbances of function or pathological states of the biliary or gastro-intestinal tract. Of these, as a result of treatment, 13 showed complete arrest of the migraine, 3 partial arrest, that is, a lessening in the intensity and frequency of the attack, and 1 case made absolutely no improvement in this particular, although improved otherwise. In addition, 9 other patients exhibited severe headaches but not of the migraine cyclic type, and all 9 of them showed complete arrest of this complaint as a result of treatment. It has appeared to us that this group associated with headaches, biliousness and "masked" infection are in earlier stages of gall-tract

disease and often amenable to this form of treatment. Conversely we have frequently noted that in the group whose diagnoses of biliary disease can be made quite clearly on analysis of history and physical findings *alone* the patient gave us histories of having these severe migraine or migranoid headaches one to ten years previously, but are no longer complaining of them in their present account of their illness. Apparently, then, when they have passed through this phase spontaneously they are in a later stage of gall-tract pathology.

Mr. J. D. E., aged forty-two years, was referred to us on April 10, 1920. For eight years he has had recurring attacks of pain or distress and a sense of gnawing and weight-discomfort in the epigastrium, and bloating with belching. The pain was referred to the back when severe and occurred one to three hours p. c., and was relieved by eating or vomiting. The attacks were always in the spring of the year.

Examination. Asthenic. Pulse, 72. Two dead molars. Gums clean. Tongue clean. Tonsils red and retracted. Heart muscle was weak. The abdomen showed no rigidity but tenderness on deep pressure over the gall-bladder point and pressure over McBurney's point elicited pain referred to the epigastrium. "Tuning-fork auscultation" suggested adhesions of the stomach to the gall-bladder region. Spinal tenderness, 3d to 6th thoracic and 10th thoracic to the left. Hemoglobin, 90 per cent. Technical findings: Marked catarrhal duodenitis; catarrhal exfoliative cholecystitis with stasis and atony. Green-black "B" bile and pure culture recovery of Streptococcus hemolyticus. Upon removal of tonsils the culture recovered only the Streptococcus hemolyticus. Vaccines of both were prepared and have been used alternately, with weekly drainage of gall-bladder. The gall-bladder atony has cleared up and general systemic improvement has followed. Streptococci are no longer recoverable from the bile by culture nor found in fresh or stained spreads, and the other abnormal findings in his bile have entirely disappeared.

Comment. This case suggested ulcer, based on the history, but biliary drainage proved the gall-bladder to be the seat of trouble, associated with duodenitis, and the subsequent response to treatment confirmed the diagnosis of "masked" infection of the gall-bladder with complete arrest of presenting symptoms, and final inability to recover the pathogenic infecting organisms on repeated culturation.

This case also illustrates the primary focus of infection in the tonsils transplanted to the gall-bladder, producing a secondary focus. It would therefore be fallacious to attempt to limit the treatment to the removal of the latter focus if the primary source of infection is ignored, unsearched for, and if found allowed to remain.

Dr. H. F. E., aged thirty-nine years, to whom we are indebted for giving us the following account of his personal experience with non-surgical biliary drainage in the treatment of acute cholecystitis complicating typhoid fever.

He was taken sick in April, 1920, with walking typhoid, during which period blood cultures were negative. He collapsed after the third week and was taken to a hospital, where he ran a typhoid course for ten weeks. He suffered a relapse after the fourth week. For three or four days previous to this relapse he had had considerable gas after meals and abdominal distention which previously had been relieved by enema. Enemas no longer removed the gas and suddenly one evening the patient was taken with acute distention in the region of the gall-bladder, at the left edge of the right hypochondrium, preceded at seven in the evening with a slight chill. There was no appreciable rise in the leukocytes. Gradually the pain became so severe that at 1 A.M. $\frac{1}{6}$ grain of morphine was given, followed by $\frac{1}{4}$ grain, without relief. The pain increased and another $\frac{1}{4}$ grain was given. The pain became so excruciating that the patient screamed loudly and begged to be put under anesthesia. Dr. Doyle was called and washed his stomach, with no relief. A duodenal tube was then passed. No relief was experienced when the tube entered the duodenum, but instant relief came within five to ten minutes after magnesium sulphate was introduced and bile began to flow. In half an hour he was perfectly comfortable. From a subnormal temperature before his attack the temperature rose abruptly during the attack to $106\frac{2}{5}°$ F. and dropped again to 100° F. immediately after biliary drainage was established. Dr. E. went to sleep with the tube in place within half an hour. The tube remained in the duodenum overnight. The bile was very dark, very tenacious, cloudy and was a deep green-black. The next day he was fairly comfortable and the tube was kept in until 8 or 9 A.M. About 18 ounces of mixed bile was recovered during the night. The tube was inserted again in the evening without washing the stomach. Bile flowed immediately after introduction of magnesium sulphate, but was not so dark. The bile was at first viscid but became progressively thinner and lighter in color as the drainage was repeated daily for four or five days, then every other day. The bile always gave positive cultures for typhoid bacilli, even up to Dr. E.'s discharge from the hospital, about six weeks later. The total number of drainages given in the hospital was about twenty-two. He went to Atlantic City immediately after his discharge, where his nurse gave him a drainage treatment two or three times a week for three weeks. Thereafter during that summer, in the White Moutains, he gave himself a treatment on three occasions. No final cultures were made from his bile. He has remained well for eight months, has been in active practice and says he feels perfectly well.

His history previous to typhoid fever was briefly as follows: He

had had no infections, except that in Pittsburgh, in 1912, when he was a hospital resident, he had two gall-bladder attacks preceded by conjunctival jaundice. Roentgen-ray examination was negative. He was in bed for ten days each time. Between 1903 and 1907 he had recurrent attacks of follicular tonsillitis, but the tonsils were not removed.

Comment. This is a most important type of case in which this method of treatment has great promise. We all know how serious operative interference may be for acute conditions arising as complications during the acute and prostrating infectious diseases. Surgery has successfully managed some of these cases but the mortality has been high. But surgery, until recently, has been the sole choice and the risk taken was warrantable. Now we have a alternative choice, which can be more safely tried, and, if successful, the operative risk is avoided.

Secondly, this case teaches the lesson of the importance of the detection and treatment of typhoid carriers, as commented on in a previous paper.[8] This has been emphasized, too, by Nichols and others[2] and later by Henes.[10] Dr. E. is not yet safely out of the woods and should be reëxamined for residual infection both for the sake of himself and of others.

Third, this case is similar in its acute picture to 2 cases, within the past two years, of acute empyema of the gall-bladder which were successfully treated by this method: One in a man who, for business reasons, positively refused the operative course advised him and the other in a woman who had such a severe cardio-renal disease as to imperatively contraindicate surgery if there was any other acceptable alternative.

If the gall tract in any given case can be made to successfully drain by this method the patient may be safely tided over the acute phases. If it cannot be successfully drained, surgery become imperative. Naturally this method should not be advocated if there are no surgical contraindications, since otherwise surgery becomes the absolute choice of procedure providing *safe* surgical skill is available.

Mrs. R., aged thirty-three years, referred to us on August 6, 1920, was operated upon eight years ago for empyema of the gall-bladder. A cholecystostomy was done but a biliary fistula developed through which she was drained constantly for *eight years*, with the exception of several weeks, when the sinus remained closed following cauterization. She has worn a dressing pad constantly, and during this period has not remained pain free for longer than a month, and usually has had recurrent attacks of the upper right quadrant pain referred around the costal margin to the right shoulder-blade every four to twelve days. Five years ago, for the relief of pain, she began to use a small silver catheter, which was introduced into her

gall-bladder every night and morning by her husband, who had become most expert with it. It was noticed that she was more liable to be pain-free when bile was recovered by the catheter, but when thick white mucus and no bile was aspirated a pain attack very quickly followed. This suggested that the cystic duct became blocked by mucus secreted by the racemose glands at the neck of the gall-bladder and a hydrops of the gall-bladder would probably have followed if this mucus could not find an exit by way of the fistula. During these pain attacks there was frequently associated chills and fever for a day or two, with stiffening of the upper right rectus. Another surgeon (who referred the case to us) had watched the patient through many such attacks for three years and had made several attempts to close the sinus tract by cauterization, but with no permanent success.

When she first presented at our office we catheterized the gall-bladder, and by means of a small syringe obtained a greenish-brown bile (with much mucopus flocculations in it) for culture and cytological examinations. The latter showed most beautifully the type of tall columnar bile-stained epithelium which we had previously seen in many other cases, and had, we think, learned to correctly classify as gall-bladder epithelium on account of its height and its tendency to break off from the basement membrane at the reticulated folds of the rugæ and to become arranged in fan-shaped masses. With this epithelium was found much inflammatory débris, pus cells and many colonies of heavily bile-stained bacteria. The following day we checked up our findings by duodenobiliary drainage and recovered the *same type bile*, with the *same cytological picture* of the mucopus floccules, and Dr. Richardson recovered from our cultures from both sources the *same bacteria* (and only them), namely, a hemolytic streptococcus and the Bacillus coli communis.

A gall-tract drainage was given every fifth day and each one was followed by an attack of upper right quadrant pain. This we have noted very frequently in our series of the more acute cases of gall-bladder inflammation and perhaps more frequently with those infected with streptococci. This seems a natural result of making the inflamed viscus empty itself, but in all of our cases, except one thus far, the pain following such drainage has become less severe until none is felt. After the third drainage and injection of vaccine, the sinus closed and *has remained closed since* (now eight months) but two days later an acute attack of pain occurred, with moderate fever, chills and leukocytosis and a surgical type of the upper right quadrant. There were no untoward developments after one week's hospital observation, and treatment was then resumed on the following basis: A duodenobiliary drainage daily for three days, then twice a week for four weeks, every seven to ten days for another month and thereafter every three weeks. An autogenous vaccine

was made and administered every fifth day, and at first gave rise to a definite focalizing gall-bladder pain, and after four months the streptococcus disappeared from our cultures and since then on seven cultures made every third week only the Bacillus coli has been recovered. We have seen this disappearance of streptococci following autogenous vaccination and drainage in twelve cases of our series. Her pain attacks persisted after each drainage for the first month, but for the past seven months she has had none. Not only has she had a complete arrest of symptoms, but there has been a general systemic improvement in endurance, in color, in bowel function, appetite, sleep and general sense of well-being. In addition, and this is the important point which we wish to stress, there has been a steady though gradual disappearance of all the abnormal cytological findings from her bile. Her gall-bladder drains readily in response to magnesium sulphate and apparently continues to function normally between treatments, and we believe now that her focus of infection has been permanently eradicated. She sailed for Italy last month, taking with her a duodenobiliary drainage outfit, and will continue to give herself a treatment (as many patients have been taught to do) once a month. They find it very easy to do. We believe it to be a good prophylactic policy for them to follow and will guard against relapses.

Comment. We have recited this case in some detail because it has been one of great interest and instruction to us: First, because we were able to obtain bile by direct catheterization from the gall-bladder for microscopic examination and culturation, and, secondly, because of our recovery by the duodenal route of the same type bile with identical cytology and bacteriology we have again satisfied ourselves that this method of diagnosis and treatment (as one of us has previously presented it) is fundamentally correct, and is, moreover, a practical and efficient procedure; and, third, that a bacterium thus isolated in pure culture, and given as a vaccine, has a definite and specific therapeutic value in closing a sinus and overcoming a focus of infection in the gall tract; and, finally, that the possibility of the specificity of the bacterium is enhanced if it gives rise to a focalizing reaction which reproduces one or more of the presenting symptoms.

During the past year we have closed successfully by this method one other case of persistent biliary fistula of months' duration, this second case being infected with Staphylococcus aureus and Bacillus coli.

Mr. M. R. E., aged twenty-nine years was referred to us on August 5, 1920. He presented historically a mixed syndrome of a gnawing pain-distress in the epigastrium, occurring two or three hours after meals, relieved by eating or alkalies, but followed by post meal-belching and upper abdominal distress. These symptoms first

appeared about one year ago and have been featured by their intermittent appearance and spontaneous total remission.

His past history brought out the following important points: He was a "blue baby" for several months, but apparently recovered without serious damage to his heart. He had been subject to recurrent attacks of tonsillitis every winter for several years. In 1918 he had a severe attack of pandemic influenza, with chiefly intestinal focalization. In 1902 and again in 1906 he had suffered attacks of typhoid fever, both apparently genuine, but not accompanied by relapse or complication. Furthermore, his story suggested there was a possible typhoid carrier in his family, inasmuch as he said that his mother had had typhoid fever three times, and one brother and sister each had had one attack. He, himself, had been subject to bronchitis for years.

On physical examination the positive findings were as follows: Two dead and many decayed teeth requiring fillings, but no root abscesses. His tonsils were badly diseased and infected. He had chronic bronchitis with musical dry rales. There was slight rigidity of the upper right rectus, but no tenderness. The gall-bladder was not palpable. By "tuning-fork auscultation" there was definite transmission of the gastric note to the left edge of the right costal margin, but not transmitted through the liver. This we have learned to interpret as being very suggestive of adhesions between the pylorus or duodenum and the gall-bladder. When the gastric note is clearly transmitted through the liver the adhesions are more liable to be denser and attached to the under surface of the liver itself.

As a result of technical examination we found that Mr. E.'s stomach had escaped organic damage, but showed a fractional curve of hypercholorhydria, with the suggestive extragastric terminal elevation. He gave evidence of an exfoliative duodenitis and a catarrhal and infected cholecystodochitis, with pericholecystic adhesions obstructing the cystic duct. Cultures from this bile recovered a hemolytic streptococcus and Bacillus coli. The roentgen-ray study of his gastro-intestinal tract was reported summarized as follows: "Duodenal ulcer with periduodenal adhesions. The gall-bladder is not visualized." We, however, were unable to develop clinical or laboratory evidence to support this diagnosis of duodenal ulcer and felt that we had to deal primarily with an infected gall tract with periduodenal-cholecystic adhesions.

As a preliminary plan of treatment following our usual custom he was referred for the necessary dental work, and his tonsils were taken out, 50 per cent of the crypts were cultured, and a pure culture of hemolytic streptococci, like that isolated from his bile, was recovered and the two were mixed and used as a vaccine.

After several therapeutic duodenobiliary drainages had been given him we noted the fact that only one out of five recovered "B" or

gall-bladder bile, and increased our conviction that the cystic duct was obstructed and, although he had made some improvement, we referred him for operation. At operation our diagnostic conception of the case was verified. He was found to have no evidence of duodenal ulcer, but running from the lateral and anterior surface of the second portion of the duodenum to the mid-region, and to the neck of the gall-bladder were fine bands of adhesions which angulated the gall-bladder at two points. The gall-bladder was long and distended and could not be emptied by digital pressure. The gall-bladder was opened and a culture taken from which the hemolytic streptococcus was alone recovered. The mucosa was reddened and granular but not of the strawberry type. The cystic duct was probed and found obstructed just below the neck of the gall-bladder at a point where the adhesions were attached. In freeing the adhesions the gall-bladder was so badly traumatized that it seemed wise to remove it. The patient made a good postoperative recovery for two months, but then partially relapsed, and, on reculturing his bile, the Streptococcus hemolyticus was again recovered, together with Bacillus coli, and the duct bile microscopically still showed the inflammatory findings of a residual duct infection. Postoperative duodenobiliary drainage was then instituted at weekly intervals and the new vaccine administered with prompt symptomatic response, and at the end of ten treatments the streptococcus disappeared from the cultures, and a month later the bile was reported sterile and has remained so since. The positive cytological picture of residual duct catarrh also cleared up by degrees and is now normal, although he has had no treatment for two months, and the patient is perfectly well and fifteen pounds heavier. It is interesting to note that the typhoid bacillus was not recovered from his bile by tube drainage or at operation.

Comment. This case again illustrates the importance of realizing that the so-called duodenal ulcer syndrome, based largely upon the history when unsupported by other clinical or laboratory data, bears an unreliable reputation and will trap the unwary or careless diagnostician. We must learn that the one- to three-hour postmeal epigastric empty distress, or so-called hunger pain, does not necessarily mean ulcer even when the pain is relieved by eating or the use of alkalies or antispasmodics, but should rather be thought of as a *mixed syndrome* in which duodenal irritation short of ulcer, with or without adhesions, cholecystitis and appendicitis, or combinations of them, must be differentially proved. Rarely, as Eusterman points out,* benign gastric tumors may simulate the so-called duodenal ulcer syndrome.

The second diagnostic lesson this case teaches is that the roentgen-ray diagnosis of duodenal ulcer cannot always be separated clearly

* Dr. Eusterman's paper has not yet been published.

from duodenal adhesions and that the final diagnosis should be made by adjusting a proper balance between the history, physical findings and the data obtained from laboratory studies.

The third diagnostic lesson taught us by this and other cases is that when we fail to recover "B" or gall-bladder bile after several attempted drainages it is strong evidence in favor of an obstructed cystic duct or a fibrous, atrophic functionless gall-bladder or one filled with stones and containing no bile. This is diagnostic evidence of great value to the surgeon when preoperatively secured.

The therapeutic lessons we learned from this case and others similar to it are:

First. That the great primary essential in the treatment of these cases, whether medically or surgically managed, is to first remove all foci of infection higher up which may have caused (or may retard the healing of) the lesion in the upper right quadrant.

Second. That this method of non-surgical biliary drainage is not therapeutically applicable to *gall-bladder* disease in which the cystic duct is obstructed in such a way that the gall-bladder is unable to discharge its fluid contents.

Third. That this method of non-surgical biliary drainage has a very large and important field of usefulness in postoperatively continuing the surgical principles of free drainage in such cases in which surgery alone has failed to eradicate all residual infection. Duodenobiliary drainage, together with the use of autogenous vaccines, will prevent many of these cases from relapsing and will relieve both the surgeon and the patient from the vexatious and dangerous necessity of reoperation.

Mrs. E. R., aged forty years, was referred to us on August 19, 1920.

Chief Complaint. Pain in the right upper abdomen radiating to the back.

Family History. Father dead; renal, aged fiftythree; mother dead, cancer of breast, aged fifty-six years.

Present Illness. Attacks of acute epigastric pains, stabbing and grinding for six years; vomiting of undigested food two or three times a week, but during the past six months the picture changed and she had had about once a month severe attacks of nocturnal colicky pain in the right hypochondrium, radiating around the right costal margin. No jaundice but sallowness at times. Frontal headache and at times occipital. Eggs and beef disagreed. She became easily tired and was drowsy most of the time. There was epigastric bloating relieved by belching and epigastric pressure gave slight relief. The pain is generally nocturnal and unrelieved by food-taking. Vomiting of food as eaten, with bile and mucus. Constipation was obstinate. Mouth negative, except coated tongue. The abdomen was diffusely tender at McBurney's point and under the right costal margin, but the gall-bladder was not palpable.

In two attempted successive biliary drainages the gall-bladder failed to drain at first, and in the second only 32 cc of dark green turbid bile were recovered. At the same time the patient had an attack of pain similar to the previous attacks. Many cholesterin crystals were found in the bile and much amorphous bile salts. Culture: Bacillus coli (heavy growth).

Urine: Negative; 90 per cent elimination of phthalein in three hours (80 per cent in two hours). Blood: Hemoglobin, 85 per cent; white blood count, 7100.

Comment. An operative decision was made for this patient on the following grounds: She presented a clear-cut picture of gall-stone colic with increasingly frequent attacks. Her diagnostic drainage suggested a partially obstructed cystic duct and showed an infected bile microscopically suggestive of cholelithiasis. We believe all definitely proved gall-stone cases with *irritable* gall-bladders and infection should be operated upon unless there are operative contraindications present which may jeopardize the life of the patient. We are still in doubt as to the wisdom of routinely insisting that definitely proved gall-stones, when quiescent and with no history of previous activity, is, *per se*, an operative necessity. We believe there is no cure for gall-stones except the knife when skilfully used, and that the presence of calculi increases the likelihood of cancer of the gall-bladder. We believe that gall-stones in the presence of active infection make the gall-bladder more irritable and increase the tendency to colic attacks and to traumatization of gall-bladder tissue which may accelerate cancerous growth. Therefore such cases more imperatively require operation. But we further believe that preoperative diagnostic drainage will be of great service to the surgeon in suggesting what may be found at operation; that the fact that obstruction of the cystic duct preoperatively ascertained will be advantageous to know; that the determination preoperatively of the presence and the nature of the infection by cultural identification (to be checked up during operation) will be information of great importance to the surgeon in guiding him in what operative procedure to adopt, and especially will this be true if the preoperative study suggests the presence of duct infection in addition to bladder infection, calculous formation or obstruction of the cystic duct.

We are especially gratified to see the publication of an article by a surgeon (Dr. Whipple[15]) endorsing these views.

Finally, we believe that no case falling in this group should fail to have a postoperative study within two months after operation, and if catarrh or infection is still demonstrable duodenobiliary drainages should be instituted and continued until normal findings are secured. Indeed, prophylactic drainage might well be given once each month to forestall a relapse even in a surgical case apparently cured. It is true that in a number of instances we have

recovered very small stones through the tube and larger stones from the sieved stool following a diagnostic drainage; but there are doubtless others left behind, especially so if faceted stones are recovered; yet we do not advocate this method in the treatment of cholelithiasis, because we see the possible danger of perforating a cystic or common duct with a stone impacted in it.

To continue: Operation on this patient early in September, 1920, disclosed a gall-bladder containing thirty-two stones, brown, hard, faceted, pea to marble size. One stone in the cystic duct partially occluded it. A cholecystostomy only was done. Culture at operation, direct from the gall-bladder, recovered Bacillus coli only.

Postoperative study, ten weeks after operation: Gall-bladder drainage gave 50 cc golden-brown, viscid bile, flowing intermittently. Microscopically: Cholesterin crystals and some amorphous salts. Culture: Bacillus coli.

Further Comment. We are presenting this case to illustrate the points that symptomatic relief is not always a cure. The removal of the stones gave symptomatic relief, but the subsequent finding of the same organism, and the same inability of the bile to hold its salts in solution, is far from a cure of the condition. All the factors that are theoretically necessary for the production of stones are still present, and there is no assurance that they will not reform. In this group of cases postoperative biliary drainage by this method, from time to time, has served to clear up the remaining evidence of disturbed physiological chemistry and bacteriology in a number of cases.

Mr. M. H. A., aged twenty-five years, was referred to us on October 25, 1920. He is by occupation a draughtsman, and his most important personal complaint was that he was afraid he would lose his position because of an overpowering drowsiness that made him fall asleep at his work. His drowsiness was so great that he could not stay awake during the most exciting play or "moving picture." With this drowsiness was a progressive sense of fatigue, noticed during the past year, and a gradual loss of mental keenness during the preceding five years. Prior to this he had considered himself in robust health until he first began to notice dizziness and mental hebetude. In March, 1917, and again a year later, he had attacks of jaundice, with no other symptom except loss of appetite, furred tongue, headache, drowsiness and constipation. Both of these attacks suggested at the time a simple catarrhal jaundice, and the cloudy urine and light colored stools cleared up in several weeks, yet he continued to have dizziness, increasing drowsiness, increasing fatigue, cloudy urine after excess of sweets and bimonthly attacks of frontal headaches and more or less slight jaundice of the scleræ. About a year ago he became more positively jaundiced, with cloudy,

reddish-brown urine, but no noticeable absence of bile in his stools. During this year he says he has grown very melancholic and pessimistic, although he has nothing to account for it. He has lost twelve pounds during the past year and now weighs 158 pounds.

Except for belching immediately after meals and avoidance of sweets, onions and coffee he had no gastro-intestinal complaints. Other than recited he had had no previous infection except recurrent tonsillitis during childhood, for which his tonsils were removed when he was seven. From the ages of fifteen to nineteen he had acne vulgaris very badly.

The salient points in his physical findings were as follows: Large frame, good musculature. The face is broad, forehead narrow and low and heavy lower jaw somewhat of the acromegalic type. The lids are puffed, the hair grows low on forehead and temples and is thick and stiff. The fingers are slender, however, with thumb moons only. The skin is quite markedly jaundiced and shows acne pustules and old scars. The scleræ and roof of the mouth are also jaundiced. Hypertrophic rhinitis and catarrhal pharyngitis. Tonsils are out and tonsillar fossæ are clean. Tongue slightly coated but firm. Gums clean. Teeth regular except one non-erupted wisdom. Posterior cervical and left epitrochlear glands are palpable. Reflexes normal. Lungs and heart normal.

Abdomen. Distinct upper abdominal fulness. No tenderness, muscle rigidity or spasm. Liver enlarged downward, the hard, rounded edge being palpable to 10 cm. below the costal margin. The spleen is greatly enlarged and hard and extends into the left abdomen to the navel. The edge is rounded rather than sharp. Splenic dulness is enlarged in its percussion area well back into the left flank.

Technical Examination: Blood Wassermann negative. Hemoglobin, 93 per cent; red blood cells, 4,740,000; white blood cells, 9500.

Polymorphonuclears, 65 per cent; lymphocytes, 25 per cent; large mononuclears and transitionals, 6 per cent; basophils, 3 per cent; eosinopils, 1 per cent. There was no change in shape of the red blood cells, but a noticeable microcytosis (common in hemolytic jaundice—Crawford). There was also an increase in skeined or reticulated red cells to 3 or 4 per cent. Coagulation time, five and a half minutes (slide and horsehair). A fragility test of his blood by Dr. E. B. Krumbhaar showed complete hemolysis up to 0.40 per cent NaCl, and partial hemolysis up to 0.60 per cent NaCl. This is a distinct lessening of both maximal and minimal resistance and points to a hemolytic factor in the production of his jaundice. This type of jaundice was also suggested in the absence of bile findings in his *urine* and its presence in the *stools*, both of which were otherwise negative.

Stomach. The fractional curve was one of hyperacidity, reaching its maximum of 110 total acidity and 80 free HCl at from seventy-five to one hundred and five minutes. No occult blood. Slight biliary regurgitation at seventy-five minutes. Normal amount of mucus. Motility normal. Fasting residuum: Study suggested an infective exfoliative gastritis.

Duodenal Examination. Disclosed an infective exfoliative duodenitis.

Biliary Drainage. When we came to an observation of his biliary drainage we encountered a type of "B" and "C" biles that we have never seen before in over 4000 examinations. The common duct was closed but opened promptly in response to magnesium sulphate. The "A" bile was a brownish-red, turbid, with increased mucus and viscosity. The transition to "B" bile was very prompt and the gall-bladder appeared to be under tension and discharged 320 cc of a greasy, thickish, paint-like bile of a deep reddish-brown color, turbid and containing many mucopus flocculations. It was delivered with a steady flow as though under pressure. Toward the end of the drainage there could be seen through the glass window in the tube *two* currents of bile, the most dependent one of heavier gall-bladder bile being of the color and consistency of red-brown paint and the upper current a transparent thinner bile, almost Burgundy red in color, similar to but darker than a hemolyzed blood Wassermann tube. This was the "C" or liver bile and also flowed rapidly. Over twelve ounces were recovered in less than an hour.

The microscopical examination of the mucopus floccules from the "B" bile showed many bile-stained oval and cuboidal cells in masses and strands and appearing to have a tubular architecture. Occasional masses of heavily bile-stained tall columnar epithelium were seen. The whole microscopic field was swarming with bacteria in masses and colony formation and the bacteria seemed to be entirely cocci. Culture from this bile gave a pure recovery of a *very* hemolytic streptococcus from which a vaccine was prepared.

Comment. This case was classified as a hemolytic jaundice with splenomegaly, catarrhal infective cholecystodochitis and biliary cirrhosis. After eleven drainages he had made remarkable progress, with a marked subsidence of his presenting symptoms. He was markedly improved in his mental state and in endurance, was keen and alert and no longer falling asleep at his work, and the jaundice was very much lessened. His liver had decreased in size so that its edge was just palpable at the costal margin and, to our surprise, his spleen was so much smaller as to be difficult of demonstration.

Dr. Krumbhaar had told us that in his opinion this was the type of case for which no medical plan of treatment had in the past proved effective and for whom a splenectomy offered the only hope. He urged our persistence in the plan of non-surgical drainage and

use of vaccines to see what might be accomplished. Up to date this man has been given about twenty-five drainages with *progressive improvement.* His skin is no longer jaundiced and there is only a subicteroidal tinging of scleræ and roof of the mouth. His biles are nearly normal in their gross appearance and the cytological picture is much improved. The liver is again of normal size, and although the splenic area to percussion is still enlarged the spleen itself is no longer palpable within the abdomen.

We are extremely interested in the outcome of this case. If the clinical improvement so far secured can be increased or made permanent over an extent of one or two years it will open up an enlarged field of usefulness of this method. While we are at present engaged upon some physiological and chemical studies on this patient a great deal of further work must be carried through before we can understand thoroughly the underlying factors concerned in producing this condition. We believe that continual duodeno-biliary drainage day and night, over a period of two or three weeks, with an interruption of a like period, (after our manner of treating chronic arthritis)[12] might accomplish a prompter and more conspicuous improvement. This plan was suggested to this patient, but declined on the grounds that he was feeling so well that he did not feel justified in absenting himself from his work.

This is one of the problem diseases of internal medicine that may be in the future succesfully combated by this method. Pernicious anemia, Banti's disease, biliary cirrhosis, toxic cholecystodochitis and hepatitis may be benefited by this plan. Diabetes has already been treated with some success.

BIBLIOGRAPHY.

1. Meltzer, S. J.: Jour. Am. Med. Assn., April, 1917, **153,** 469.
2. Nichols, Simmons and Stimmel: Jour. Am. Med. Assn., August 30, 1919, **73,** 680.
3. Lyon, B. B. Vincent: Jour. Am. Med. Assn., September 27, 1919. **23,** 980.
4. Lyon, B. B. Vincent: Med. Clin. North America, March, 1920, **3,** 1253.
5. Lyon, B. B. Vincent: Am. Jour. Med. Sci., April, 1920, **159,** 503.
6. Lyon, B. B. Vincent: New York Med. Jour., July, 1920, **112,** 23, 56.
7. Cheyney, William Fitch: Am. Jour. Med. Sci., October, 1920, **160,** 469.
8. Lyon, B. B. Vincent: Am. Jour. Med. Sci., October, 1920, **160,** 515.
9. Brown, G. E.: Jour. Am. Med. Assn., November 20, 1920, **75,** 1414.
10. Henes, Edwin: Jour. Am. Med. Assn., December 25, 1920, **75,** 1771.
11. Editorial: British Med. Jour., January 8, 1921, p. 58.
12. Lyon, B. B. Vincent: Med. Clin. North America, January, 1921, **4,** 1153.
13. Einhorn, Max: New York Med. Jour., February 19, 1921, **113,** 313.
14. Smithies, Frank: Illinois Med. Jour., April, 1921.
15. Whipple, A. O.: Ann. Surg., May, 1921, **73,** 556.
16. Simon, S. K.: Southern Med. Jour., June, 1921, No. 6, vol. **14.**
17. Crohn, Reiss and Radin: Jour. Am. Med. Assn., June 4, 1921, **76,** 23.
18. Rost (of No. 1):

THE DIAGNOSIS OF PERITONITIS AND PERITONEAL TRANSUDATES IN INFANTS BY MEANS OF ABDOMINAL PUNCTURE WITH THE CAPILLARY TUBE.

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In a preliminary communication a method was demonstrated which had been used in the diagnosis of a few cases of peritonitis and peritoneal effusion.[1] Since then the technic has been modified and the method has passed the experimental stage.

The original procedure consists in puncturing the skin with a metal needle, and through the opening thus made, inserting into the peritoneal cavity a glass needle with a capillary bore. Fluid rises in the glass tubing by the force of capillarity. In order to obtain larger amounts the tube was bent and a bulb was blown for the collection of the fluid. The objections to using glass needles are obvious, and the only advantage that still remains over the modification to be described is that a larger amount of fluid may be collected in the bulb of the glass needle. This advantage is insignificant compared with the greater safety in the use of the metal cannula, trocar and capillary tubing.

Only the latest, and thus far the most satisfactory, instrument, will be described.[2] It consists of a trocar-cannula and glass capillary tubing, and is shown in diagram in Figs. 1 and 2. The cannula is held by a handle and the shoulder is as short as it can be made. The shaft of the cannula is 17 gauge and $\frac{1}{2}$ inch in length. It has a sharp beveled point, and the trocar is made to correspond.[3]

Most of the capillary tubes were prepared by the author from glass tubing 4 mm. in diameter. This tubing was drawn out in the Bunsen flame and varied in thickness. Only those parts were used that fitted the shoulder, or rather the proximal part, of the shaft, and the tubing was cut off so as to protrude 1 or 2 mm. from the end of the cannula. The purpose of this technic is to prevent breaking the capillary tube within the peritoneal cavity. The cannula with the capillary tube prepared in this way is illustrated diagrammatically in Fig. 3. The capillary tube impinges upon the wall of the cannula at *A*. After the tubing is safely inserted into the cannula as far as it will go a break, if it occurs at all, will take

[1] Denzer, B. S.: Am. Jour. Dis. Children, August, 1920, **20**, 113.

[2] The instrument was made by the Randall Faichney Company, of Boston, Mass.

[3] A cannula with a flat end and trocar with an arrow-head point, similar to the larger instruments for abdominal paracentesis, was tried but was found unsatisfactory.

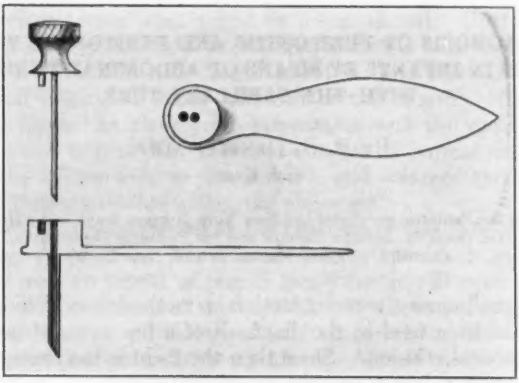

FIG. 1.—Trocar and cannula and top view of cannula. Semidiagrammatic cross-section.

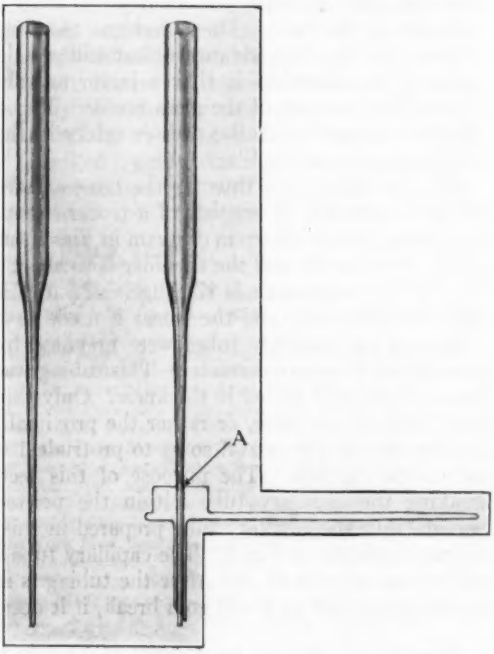

FIG. 2 FIG. 3

FIG. 2.—Capillary tube as prepared by author.
FIG. 3.—Cross-section of capillary tube fixed in cannula at *A*.

place above the point *A*, and the lower fragment, firmly fixed in the shaft, can be withdrawn with the cannula. Some of the capillary tubing was prepared by glass blowers (Fig. 4).

When glass tubing is used repeatedly the utmost precautions are necessary to obtain clean surfaces. As capillarity depends upon the capacity of the liquid to moisten the surface of the tube a minute film of fatty material might check the rising column of fluid. Cleaning fluid, hot water, alcohol and ether are used in obtaining clean glassware.

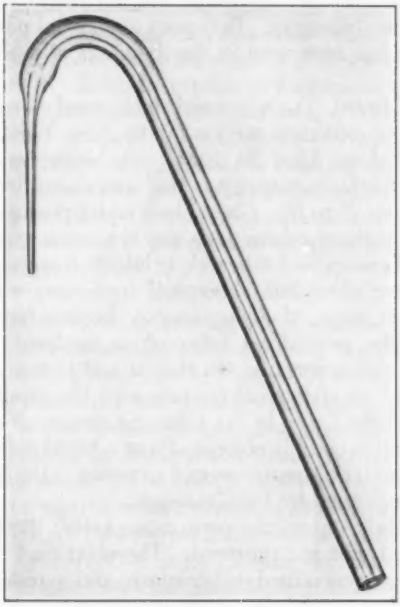

FIG. 4.—Capillary tube prepared by glass-blower.

The technic with the trocar-cannula and capillary tube is as follows: After sterilization of the skin and the usual precautions to determine bladder distention the point of the trocar-cannula is thrust through the skin and into the peritoneal cavity. The trocar is withdrawn and the capillary tube inserted as far as it will go. It is advisable to wait a few minutes and turn the needle in various directions before concluding that there is no fluid. Possibly a bit of omentum or the wall of the intestine may temporarily block the capillary tube; or when there is only a small amount of fluid this momentary wait and the straining and crying of the infant may distribute it over the entire peritoneal cavity. Any place on the abdomen except those parts covering a solid viscus may be used.

As a rule the midline just below the umbilicus is the site chosen, though punctures have been done in the iliac fossæ.

Peritonitis. The peculiar difficulties encountered in the diagnosis of peritonitis in infancy are too well recognized to demand lengthy discussion. Some of the classical signs and symptoms of peritonitis in adult life, such as pain, localized tenderness, distention and paralytic ileus, are either absent or difficult to elicit, and even when present they may be ascribed to minor gastro-intestinal disturbances, of which they are likewise characteristic signs. Standard textbooks on pediatrics and special studies on peritonitis in infancy[4] emphasize these difficulties. In 5 cases abdominal pucture with the capillary tube has been used in the diagnosis of peritonitis.

Case I.—Edward T., a colored boy, aged three years, was admitted to the pediatric service of the New York Nursery and Child's Hospital on April 20, 1920. No history was obtainable. On admission the temperature was 103° and thereafter showed wide variations—from 2° to 6°. Chest signs and a positive von Pirquet pointed to pulmonary tuberculosis and the septic type of temperature suggested generalized tuberculous infection as well. On May 5, two weeks after admission, abdominal tenderness was first noted. The abdominal signs, though variable, became more and more definite, but the generalized tuberculosis rendered the diagnosis of acute peritonitis uncertain. On May 16 and 17 vomiting occurred, and on May 17 an abdominal pucture with the capillary tube was done. Whitish fluid rose in the tube and smears showed pus cells and Gram-positive cocci in chains. From a blood culture taken the same day a hemolytic streptococcus was grown. On May 18 a laparotomy was performed by Dr. Truesdale.

There was fluid pus in the peritoneal cavity; the appendix was swollen and red, but not ruptured. The child died the same day, and at autopsy generalized tuberculosis and purulent peritonitis were found.

Case II.—Baby L., a colored infant, aged two months, weighing six pounds six ounces, was admitted to the hospital on July 19, 1920. As the baby was a foundling the history was incomplete. At the first examination, Dr. Anderson, the resident physician, made the following note: "The baby presented the usual picture of a true marantic—worn, anxious expression; thin, emaciated body; dry and inelastic skin." At first the baby's abdomen was distended, but during the twenty-four hours after admission it became distinctly softer. Marasmus, with the possibility of luetic infection, was the diagnosis considered.

[4] Abt, I. A.: New York Med. Jour., 1917, **105**, 769. Dowd, C. A.: Ann. Surg., 1908, **48**, 821.

Abdominal puncture was done with the glass needle. A white milky fluid rose in the tube and showed on smear Gram-positive cocci in chains. The following day a laparotomy was performed. The baby's condition was too critical to permit anything more than the evacuation of a large quantity of pus and drainage of the peritoneal cavity. Death occurred on the day of operation The autopsy showed a diffuse purulent peritonitis. No focus of infection or portal of entry could be found, and the case must be classified as a so-called idiopathic peritonitis in infancy.

This case is particularly interesting because there were no signs of peritonitis. An abdominal tap was done merely because this procedure had been adopted in all acutely ill cases when the diagnosis was in doubt. Baby L. typifies peritonitis in early infancy. Such infants show the signs of marasmus only, and there is nothing either in the history or examination to direct attention to the abdomen. Confronted with this problem the clinician cannot find adequate grounds for suspecting peritonitis; at the same time he cannot exclude such a possibility. Under these circumstances a procedure that reveals the presence of an exudate or gives assurance of its absence may be very helpful.

Case III.—Baby V., an infant, aged two months, was admitted to the hospital on January 20, 1921, suffering from a lobar pneumonia of three days' duration. On January 27 an empyema of the right chest was discovered and drainage instituted. The following day the abdomen was distended and an abdominal puncture was done. Purulent fluid was obtained and Gram-positive cocci in pairs were found on a smear. The baby's condition was most critical and the usual therapeutic measures offered little hope. At the suggestion of Dr. Witt, of the resident house staff, 25 cc of antipneumococcus serum, Type I, were injected into the peritoneal cavity. The child died the same day, but an autopsy could not be obtained. The culture of the peritoneal fluid developed what was apparently a pneumococcus, but a contaminating organism prevented its isolation and typing.

Case IV.—Baby M. was delivered on the obstetrical service of the New York Nursery and Child's Hospital February 26, 1921, weighing at birth six pounds thirteen ounces. The infant was transferred to the pediatric service, with a history of a steady decline in weight, refusal of food, vomiting and abdominal distention. After temporary improvement these symptoms recurred, and in addition, on March 21, pus was noted exuding from the umbilicus. The right iliac fossa was chosen as the site for the abdominal tap in order to avoid contamination by the purulent process localized about the umbilicus. Purulent fluid was obtained, but no organisms could be found on the smear, and the culture was sterile. Operation was

considered inadvisable and the baby died on March 24. At autopsy the ascending colon was found to be covered with loose vascular fibrinous adhesions—a localized plastic peritonitis. Whether there was also a generalized peritonitis could not be determined because of the flooding of the abdominal cavity by the intestinal contents, due to a rupture of the duodenum.

Case V.—Francis R., an infant, aged two months, was admitted to the hospital on March 28, 1921, because of vomiting, refusal of food and an infected umbilicus. On examination the umbilicus was found to be red; the edges pouted and a drop of pus could be expressed. A mass was felt surrounding the umbilicus and extending toward the left flank. An abdominal tap was done. Very little fluid was obtained and two capillary tubes had to be passed into the cannula to get sufficient exudate for two smears and a culture. The smears were crowded with pus cells and a very few organisms in pairs were found. A laparotomy was performed. The peritoneum was found to be thick and indurated, but *there was apparently no free fluid exudate.* The cells of intestine were very red and injected and covered with a loose fibrin. One pole of the spleen was adherent to the peritoneum in the umbilical region and a probe could be passed through the infected umbilicus into the peritoneal cavity. The abdomen was drained. The child died on the day on which he was operated, but an autopsy could not be obtained.

Abdominal puncture in this case was particularly instructive, in that it demonstrated how small an exudate may be revealed by the capillary tube. Although enough fluid was obtained with the capillary tube for smears and culture no free fluid was found at operation but merely a loose edematous fibrin covering the intestinal coils.

The therapy of peritonitis in infancy is extremely unsatisfactory. Indeed, many cases are discovered only at autopsy. The procedure suggested offers the hope of early diagnosis, and this, in turn, may develop more adequate therapy.

Marasmus. Fluid was found by abdominal puncture in the peritoneal cavity in 7 of 12 marantic infants (Chart I). As a rule the fluid was clear; only those specimens that contained 1700 or more cells showed a granular turbidity. There is nothing characteristic concerning the cellular elements, which are chiefly lymphocytic. The albuminous content, as judged by the appearance of the smears, must be low; the picture is quite different from that of many pus cells in a heavy albuminous matrix observed in peritonitis.

No reference to an excess of peritoneal fluid in marasmus could be found in the literature.[5] It is hardly conceivable that the occur-

[5] Finkelstein and others mention the occurrence of "hydrops," but this refers to a subcutaneous accumulation of fluid.

CHART I.—ABDOMINAL TAP IN MARASMUS.

Name.	Age.	Weight.	Diagnosis in addition to marasmus.	Condition of abdomen.	Result of tap.	Cell count.	Remarks.
Virginia K.	4	4	.....	Scaphoid	0		
Susan H.	5	8¼	Tuberculosis	Not distended	0		
John M.	2½	5¾	.....	Slight distention	0		
John S.	4¾	8 1/16	Intoxication	Not distended	0		
Lucinde, P.	3½	7¼	.....	Not distended	0		
James P.	3½	5½	.....	Flat	+	860 cells per c.mm; 100 counted, all lymphocytes	
Agnes H.							
July 10, 1920	3	6¾	.....	.....	0	.....	Two intravenous and one intraperitoneal injection before tap.
Aug. 4, 1920	3¾	6	.....	Slight distention	+	19 cells per c.mm.; large epithelial? cells	No parenteral fluids for three weeks prior to tap.
Aug. 18, 1920	4	5¼	.....	.....	+	2600 cells per c.mm.; polynuclears, 40 per cent; lymphocytes and "epithelial," 60	Two hypodermoclyses and one intravenous but *no intraperitoneal injections* given.
John H.	3½	6⅞	.....	Slight distention	+	Polynuclears, 14 per cent; lymphocytes, 86 per cent	
Catherine O'L.	3½	6¼	.....	Soft; not distended	+	290 cells per c.mm.; polynuclears, 81 per cent; lymphocytes, 19 per cent	
Cynthia L.	4½	6¼	Rickets; tuberculosis suspected	Slight distention	+	850 cells per c.mm.; polynuclears, 9 per cent; lymphocytes, 91 per cent	
William W.	3½	5	.....	Slight distention	+	1700 cells per c.mm.	
Joseph B.							
Aug. 18, 1920	5	4¾	.....	.....	+	630 cells per c.mm.; polynuclears, 20 per cent; lymphocytes, 80 per cent	
Oct. 11, 1920	7	5¾	Bronchopneumonia	.....	+	2300 cells per c.mm.; polynuclears, 4 per cent; lymphocytes, 75 per cent; "epithelial," 21 per cent	

rence of a large ascites could have been constantly overlooked in all the previous careful pathological studies. Our own autopsy protocols during the past months, when our interest was centered on this question, do not record appreciable quantities of peritoneal fluid in marantic infants. And, indeed, the results reported here do not imply the presence of a large ascites. This method—the use of the capillary tube—demonstrates very slight deviations from the normal. In the normal infant no fluid can be found by this procedure,[6] and under conditions simulating an effusion, Denzer and Anderson have found that the capillary tube shows the presence of from 5 to 15 cc of free peritoneal fluid.[7] Furthermore, there is no evidence clinically of a large ascites; neither fluid wave nor shifting dulness could be elicited in our marantic infants. Thus all the available data suggest that the transudate demonstrated by the capillary tube in marantic infants is extremely small.

The clinical significance of this transudate is not apparent. There is no relation between the occurrence of fluid and the severity of the disease. Likewise, there are no constant physical findings associated with the presence of an ascites. As mentioned previously, there is not sufficient fluid to produce the usual signs of ascites, nor can distention be correlated with the peritoneal transudate. In only one case in which a positive tap was obtained had an intraperitoneal injection been done prior to the puncture.[8] However, the ascites is sufficiently constant to be considered part of the pathological picture of marasmus.

Speculation as to the role which ascites plays in marasmus would involve the whole question of its pathogenesis, and that in turn the complicated problem of water metabolism. Such speculation would probably be fruitless, and it therefore seems advisable merely to record the fact that in a certain percentage of marantic infants an excess of peritoneal fluid is found.

Rickets. In 4 of 8 cases of rickets abdominal tap showed the presence of fluid in the peritoneal cavity (Chart II). In one case (Marie O'D.) the glass needle was used and 1 cc of fluid collected. The cells range in number from 100 to 1000. A differential smear shows a predominace of lymphocytes; the microscopic picture, however, is not characteristic and cannot be distinguished from that found in marantic infants.

The series is not sufficiently large to warrant conclusions concern-

[6] Writers on the anatomy and physiology of the peritoneum agree that there is merely enough peritoneal fluid to lubricate the abdominal contents—that normally there is no "free" peritoneal fluid. Indeed, no analyses of "normal" peritoneal fluid have ever been made because it is impossible to collect enough for chemical examination.

[7] The Absorption of Fluid Injected into the Peritoneal Cavity, Am. Jour. Dis. Children, June 2, 1921, **21**, 565.

[8] Agnes H. received an intraperitoneal injection three weeks prior to the first positive tap.

ing the cause of the ascites. The occurrence of pot-belly in most of the cases that showed free fluid suggests that the mechanical and circulatory derangement incident to the large abdomen may play some part in the development of the ascites. However, this is merely an impression, and further work will be necessary both to determine the incidence of free fluid in rickets and to explain its pathogenesis.

CHART II.—ABDOMINAL TAP IN RICKETTS.

Name.	Age.	Weight.	Pot belly.	Result of tap.	Cell count.
Isaac S. . .	11	14¾	Very slight	+	Small amount; enough for few smears only.
Stewart, S. . .	5	11½	None	0	
David D. . .	4	27	None	0	
Arnold M. . .	19	....	Moderate	0	
Doris J. . .	17	17	Very slight	0	
Marie O'D.					
Sept. 20, 1920	6	8½	Very marked	+	350 cells per c.mm.; lymphocytes, 85 per cent; polynuclears, 15 per cent.
Mar. 10, 1921	11	....	Very marked	0	
Leon T. . .	4	9¾	0	+	1000 cells per c.mm.; lymphocytes, 95 per cent; polynuclears, 5 per cent.
Hazel R. . .	8	11	Marked	+	

Summary. Five cases of peritonitis are presented in which abdominal puncture and the capillary tube were of service in establishing the diagnosis. The same method has revealed free fluid in the peritoneal cavity of cases of rickets and marasmus, a finding which, as far as I have been able to determine, has not been recorded previously. These observations on peritoneal inflammations and transudates are not numerous enough to warrant sweeping generalizations. They are important because they indicate that a procedure which demonstrates minute amounts of fluid in the peritoneal cavity may be helpful in answering many questions of practical and experimental interest—the initial response of the peritoneum to infectious and other irritants, the question of peritoneal absorption and the therapeutic use of sera in pneumococcic infections. The method of abdominal puncture with the use of the capillary tube has passed the experimental stage; a larger experience is necessary to disclose its possibilities and define its limitations.

I wish to thank Dr. A. F. Anderson and Dr. D. B. Witt, respectively resident and assistant resident physicians at the New York Nursery and Child's Hospital, for their kind coöperation in the selection of some of the cases and the performance of the punctures.

SOME STATISTICS CONCERNING PNEUMONIA AND EMPYEMA IN CHILDREN.

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This report was compiled at the request of Dr. J. P. Crozer Griffith, who was interested in the incidence of empyema after hospital-treated pneumonia. The total number of cases diagnosed as pneumonia in the children's ward of the University Hospital, Philadelphia, in the years 1900 to 1918 inclusive was 611. Children are admitted to this ward up to the age of thirteen years. The series includes the cases admitted with a primary pneumonia, those in which pneumonia occurred as a complication and influenzal pneumonias. I have excluded the cases of empyema reported in a previous paper on this subject which were admitted to the hospital on the surgical service.

The statistics of pneumonia which were necessarily collected in the material for this report are of enough significance to warrant their inclusion.

The frequency of the type of pneumonia is given in Table I. In the pneumonia of children it is often difficult to state definitely the type of the process, therefore the following figures are only approximately correct. Some of the cases might have been placed in the other group by another clinician.

TABLE I.—INCIDENCE OF PNEUMONIA.

Bronchopneumonia	274
Croupous pneumonia	312
Non-specified	25
Total	611

In Table II the incidence of broncho- and croupous pneumonia is given according to the age and sex. Charts I and II graphically express this. There is no distinction drawn in the admission of males and females to the children's ward. The total admissions to the ward in two years chosen at random showed a greater number of females than males, therefore the predominance of males in both the broncho- and croupous pneumonias cannot be ascribed to sex preference in admission or to the occasional quarantine of the ward to females because of outbreaks of vaginitis. In both types of pneumonia there is a rise in incidence during the second year. The increase in the percentage at this age is enough to be of some significance.

The well-known fact that bronchopneumonia is more frequent than croupous in infancy is well brought out by these figures, there being a difference of 12.8 per cent in the first six months and 8.2 per cent in the last six months of the first year. After the fourth

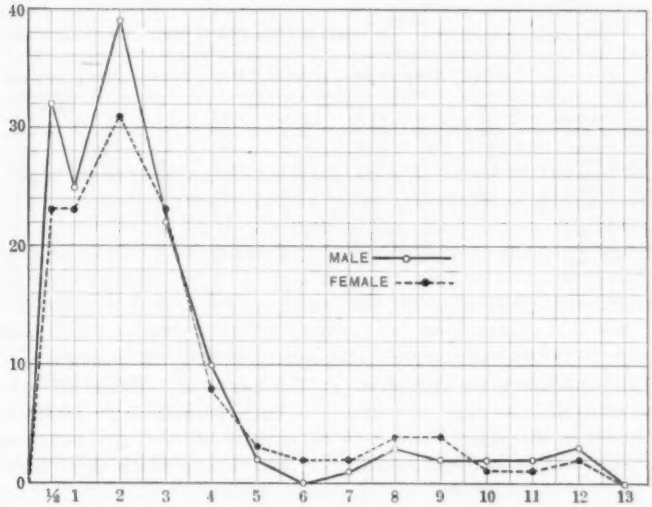

CHART I.—Age and sex incidence of bronchopneumonia.

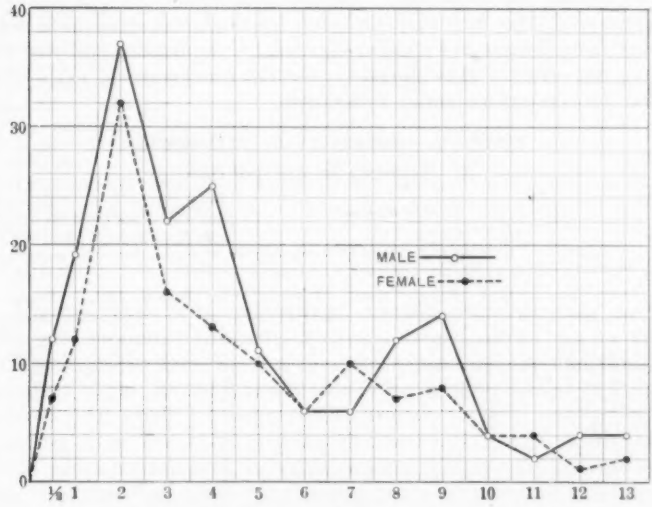

CHART II.—Age and sex incidence of croupous pneumonia.

year bronchopneumonia was relatively infrequent in this series of cases.

TABLE II.—AGE AND SEX INCIDENCE OF PNEUMONIA.

Age.	Bronchopneumonia.				Croupous pneumonia.			
	No. of cases:		Percentage of total:		No. of cases:		Percentage of total:	
	Male.	Female	Male.	Female.	Male.	Female	Male.	Female.
1 to 6 months	32	23	22.3	18.1	12	7	6.7	5.3
6 mo. to 1 yr.	25	23	17.4	18.1	19	12	10.6	9.09
1 to 2 years	39	31	27.2	24.4	37	32	20.7	24.2
2 to 3 years	22	23	15.3	18.1	22	16	12.3	12.1
3 to 4 years	10	8	6.8	6.2	25	13	14.04	9.8
4 to 5 years	2	3	1.3	2.3	11	10	6.1	7.5
5 to 6 years	0	2	0	1.7	6	6	3.3	4.5
6 to 7 years	1	2	0.6	1.7	6	10	3.3	7.5
7 to 8 years	3	4	2.09	3.1	12	7	6.7	5.3
8 to 9 years	2	4	1.3	3.1	14	8	7.8	6.05
9 to 10 years	2	1	1.3	0.78	4	4	2.2	3.02
10 to 11 years	2	1	1.3	0.78	2	4	1.1	3.02
11 to 12 years	3	2	2.09	1.7	4	1	2.2	0.75
12 to 13 years	0	0	0.00	0.0	4	2	2.2	1.5
Total	143	127			178	132		

The mortality for the series is 30.2 per cent. Table III gives the mortality by age and sex. In both varieties the mortality percentage decreases, with two exceptions as the age increases. This percentage has been omitted for the years in which the number of cases in our series was so small as to make the results misleading. There is a marked contrast in the total mortality in broncho- and croupous pneumonia, the mortality percentage for the former being 39.4 and for the latter 18.3. One obvious reason for this marked difference is the fact that bronchopneumonia occurred as a terminal complication in a number of cases. Complicating empyemata have not affected this mortality, for the occurrence of empyema after bronchopneumonia is infrequent.

TABLE III.—MORTALITY IN PNEUMONIA.

A. Mortality by Age and Sex.

Age.	Bronchopneumonia.				Croupous pneumonia.			
	No. of deaths.		Mortality percentage		No. of deaths.		Mortality percentage	
	Male.	Female	Male.	Female.	Male.	Female	Male.	Female.
1 to 6 months	18	17	56.2	73.9	5	4	41.3	57.1
6 mo. to 1 yr.	14	14	56.0	60.8	7	4	36.8	33.3
1 to 2 years	16	12	41.02	36.5	10	8	27.02	25.0
2 to 3 years	6	12	27.2	52.1	3	3	13.6	18.7
3 to 4 years	0	0	.....	.....	4	1	16.0	7.8
4 to 5 years	0	0	.....	.....	2	0		
5 to 6 years	0	1	.....	.....	1	0		
6 to 7 years	0	0	.....	.....	0	1		
7 to 8 years	0	2	.....	.....	1	0		
8 to 9 years	1	3	.....	.....	1	2		
9 to 10 years	1	0	.....	.....	0	0		
10 to 11 years	0	1	.....	.....	0	0		
11 to 12 years	2	0	.....	.....	0	0		
12 to 13 years	0	0	.....	.....	0	0		
Total	58	62			34	23		

B. Group Mortality.

Age.	Bronchopneumonia.			Croupous pneumonia.		
	Number of		Percentage of deaths.	Number of		Percentage of deaths.
	Cases.	Deaths.		Cases.	Deaths.	
Under 2 years	173	91	52.6	119	38	31.9
2 to 5 years	68	18	27.9	97	13	13.4
5 to 13 years	29	11	37.9	94	6	6.3

Some prognostic significance has been attached to the location of the pneumonia process in the lobar pneumonia of adults. For this reason Table IV is included. The mortality is highest in the cases in which one entire lung is involved, the right side showing the higher mortality. The right upper lobe is more frequently involved and has a higher mortality than the left upper lobe, while this is reversed for the bases.

The sites of the lesions in the cases of bronchopneumonia have not been tabulated because almost invariably there were areas of pathology in both lungs.

TABLE IV.—LOCATION OF THE LESIONS IN CROUPOUS PNEUMONIA.

	Number of times involved.	Deaths.	Percentage of deaths.
Left upper lobe	22	1	4.5
Left lower lobe	63	7	11.1
Entire left lung	31	7	22.5
Right upper lobe	68	6	8.8
Right lower lobe	51	5	9.8
Right middle lobe	6	0	
Entire right lung	45	16	35.5
Both apices and left base	4	2	
Both apices	3		
Left apex and right base	2	1	
Right upper and middle lobes	2		
Entire left lung and right apex	2	1	
Whole right lung and left base	1	1	

The difference in the percentage of empyemata following broncho- and croupous pneumonias cannot be accounted for by the difference in the total number of cases. However, the fact that a number of the bronchopneumonias were terminal must be considered. In Table VI a correction is made for this fact by subtracting from the total number of cases of bronchopneumonia those which died during the acute process. Although the percentage of empyemata after bronchopneumonia is lower the mortality in this type of empyema is much higher.

TABLE V.—FREQUENCY OF EMPYEMA IN PNEUMONIA.

		Per cent.
Number of empyemata following bronchopneumonia	5	1.8
Number of empyemata following croupous pneumonia	22	7.5
Number of empyemata following unspecified pneumonia	12	
Total number of empyemata in 611 cases of pneumonia	39	

TABLE VI.—CORRECTED PERCENTAGE OF INCIDENCE OF EMPYEMA.

Percentage of empyemata after bronchopneumonia (deaths during acute pneumonia process substracted)	3.14
Same correction for croupous pneumonia	8.59

TABLE VII.—MORTALITY IN POSTPNEUMONIC EMPYEMA.

		Per cent.
Number of deaths following bronchopneumonia empyemata	4	80.0
Number of deaths following croupous pneumonia empyemata	8	36.3
Total number of deaths in 39 cases of empyema	15	38.4

A slight discrepancy in a comparison of the figures of the various tables is due to the omission of cases in which all the data necessary was not present in the history.

UNKNOWN FORMS OF ARTERITIS, WITH SPECIAL REFERENCE TO THEIR RELATION TO SYPHILITIC ARTERITIS AND PERIARTERITIS NODOSA.

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Comparatively little is known about arteritis and its significance if we disregard syphilitic endarteritis, which is well known, and tuberculous arteritis in the meninges associated with exudation, which is the dominant feature. Otherwise but little has been written about arteritis until rather recently. According to Spiro,[1] French authors, and later Wiesel and v. Wiesner, described peculiar inflammations or rather necroses in the small arteries, particularly in the heart, in measles, scarlet fever, diphtheria, suppurative processes, etc., which result in scars and are believed to favor the development of coronary sclerosis, but apparently these observations have attracted but little attention. More recently the vascular changes in infections and intoxications have been studied more closely. Thus Herzog[2] describes the following changes in poisoning with illuminating gas: Hyaline swelling of the walls of the small

[1] Virchow's Arch., 1920, No. 227.
[2] München. med. Wchnschr., 1920, No. 19.

arteries in the brain with proliferation of the endothelium and hyaline thrombosis, followed later by calcification and softening of the brain tissue. Similar changes with calcification have been described as occurring quite early by Geipel and Schmorl,[3] the small arteries in the lenticular nucleus being especially involved. Similar changes may occur in other forms of poisoning, *e. g.*, hydrocyanic acid, salvarsan and phosgen gas, but it really does not concern any arteritis.

In various infectious diseases inflammatory vascular changes may occur, as seen especially in the cerebral vessels in influenza with hemorrhages, which, however, seem to depend largely on degenerative changes.[4] Markus[5] describes infiltration with cells in the wall of the vessels in the pia in influenza, and Stoerck and Epstein[6] describe necrosis and degeneration with reparatory processes in influenza, resembling the changes in arteriosclerosis. Of greater interest are the changes that have been found in the vessels of the skin in typhus by Frankel[7] and others. Nicol[8] describes these changes as involving the capillaries and precapillary arteries in most of the organs, with partly exudate, partly proliferative changes as well as necrosis. Inflammatory and degenerative changes occur also in the small vessels in the skin in epidemic meningitis, and Weiss and Stufeland[9] describe certain changes in the capillaries of the skin in scarlet fever.

While engaged in the examination of microscopic preparations from a large amount of anatomical material I met with occasional peculiar lesions in the vessels that do not correspond to the usual forms, and on this account I have thought it worth while to describe some of the cases with some detail.

Case I.—*Idiopathic Renal Hemorrhage.* This concerns a kidney which was removed from a man, aged twenty-two years, who for about one year had suffered from frequent hemorrhages from the one kidney and later from pain. Macroscopically the kidney appeared normal, but microscopically there were found necrotic foci throughout the kidney, in the center of which were arteries with swollen walls and narrowing of the lumen. The swelling was due to proliferation of the intima and to hyaline changes in the connective and elastic tissue, while the surrounding renal tissue frequently was necrotic, there being, however, no sign of inflammation.

The cause and nature of the changes in the arteries were obscure. Syphilis was excluded and it hardly concerned arteriosclerosis.

[3] München. med. Wchnschr., 1920, No. 43.
[4] Harbitz: Norsk. Mag. f. Lagevidenskapen, 1920.
[5] Ztschr. f. Neurol. u. Psych., 1920.
[6] Frankf. Ztschr. f. Pathol., 1920, No. 23.
[7] München. med. Wchnschr., 1914, 1915, 1917.
[8] Ziegler's Beiträge, 1919, No. 65.
[9] Ibid., 1918.

The case might be regarded as a local form of periarteritis nodosa, especially in view of the necroses in the media and the proliferation of the intima. That the lesion of the arteries, which involved also vessels in the papillæ, was the cause of the hemorrhage seems altogether reasonable, and in that case it hardly would be correct to speak of the case as one of "idiopathic hemorrhage," as the hemorrhages had an organic basis.

CASE II.—*Purpura Rheumatica.* This concerns a man, aged forty years, who died with the clinical picture of "purpura rheumatica" about two months after the beginning of the illness. At postmortem there was found extensive thrombosis (inferior vena cava, in the left iliac and the left femoral vein, hepatic vein with infarct in the liver, and also in several sinuses of the dura with large hemorrhagic infarcts in the brain). In the skin there was no evident exanthem, but extensive infiltrations of leukocytes, lymphocytes and red corpuscles as well as pure hemorrhages. There was also extensive changes, in the smaller bloodvessels and arteries as well as veins, with cellular infiltrations in the walls and necrosis. The intima was swollen and there was often thrombosis. These changes were most marked in the arteries, medium sized and small. The veins were not so markedly involved, but there was more or less necrosis and infiltration as well as thrombosis.

In this case syphilis may be excluded. The cutaneous infiltrations and the thrombosis were more extensive than is the case in exanthematic typhus, a disease that so far as known has not occurred in Christiania for many years. As regards periarteritis nodosa it should be noted that there were no typical nodular formations in the walls of the vessels and that the infiltrations were larger and more extensive than is the case in that disease. Hence it seems most reasonable to assume the presence of some unknown form of infection. Bacteria were not demonstrable by the usual methods.

CASE III.—*Peculiar Disease of Cerebral Arteries* (Figs. 1 to 3) A woman, aged twenty-six years, of doubtful habits. She had suffered much with headache since early in life; during the last two years she had had attacks of fainting off and on, and about a year and a half ago she received a blow to the head during such an attack. In the autumn of 1917 the hands became tremulous; even earlier she had had double vision and sometimes vestibular attacks, with vomiting as well as convulsive movement of the face. In the autumn of 1918 she had influenza and became worse afterward, with pain in the legs, difficulty in walking and convulsive attacks of a hysterical nature. In March, 1919, she was examined by Dr. Svenson, who reports as follows: Dull; rather stuporous; somewhat disoriented; speech monotonous; eyes normal; no symptoms on the part of the cranial nerves, pons or bulb. Reduced strength

in the arms; ataxia; spastic paraparesis of both legs with increased patellar reflexes and positive Babinsky sign; Romberg's symptom present; uncertain, spastic walk, but no disturbances of sensibility.

She became bed-ridden, with increasing stupor, headache, choked disk and increasing paresis in the extremities.

The disease was first regarded as a multiple sclerosis, but later, as signs of increasing brain-pressure developed, a tumor of peculiar localization and secondary hydrocephalus was considered. The patient became finally completely comatose, with muscular rigidity, fever, albuminuria and pneumonia. Death on May 19, 1919.

FIG. 1.—Extensive infiltration in the bottom of a sulcus, especially about the arteries, whose walls are thick and partly necrotic; some giant cells.

Only the brain was examined. There was injection of the membranes. In the floor of the lateral ventricles, particularly the left, were areas of a solid, rather tumor-like infiltrations; in the central ganglia were recent areas of hemorrhage, of the size of hemp seeds, and in the centrum semiovale on the right side was a hemorrhage as large as a hen's egg, the surrounding tissue being apparently hardened; there were diffusely infiltrated areas in the corpus callosum also.

The microscopic examination revealed an inflammatory process in the pia arachnoid and in the brain closely related to the bloodvessels, particularly the arteries, and following the bloodvessels from the pia inward into the brain substance. The changes were present seemingly everywhere, also at the base and in marked degree in the central ganglia. There was a remarkable widening of the bloodvessels with hemorrhagic infiltration in various places in the brain. In the pia arachnoid the inflammation was closely related to the smaller arteries and their branches into the cortex, there being no diffuse changes. The inflammatory cells were principally lymphocytic. The process extended inward from the sulci;

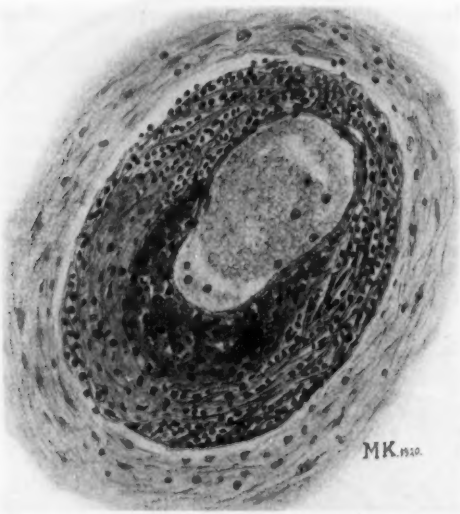

FIG. 2.—A smaller arterial branch in the surface of the brain severely infiltrated, structure not clear, partly obliterated, necrosis of intima and media.

the veins were dilated and the walls infiltrated with lymphocytes, usually diffusely, but the arterial walls were more involved, being thickened, infiltrated with lymphocytes and leukocytes as well as larger cells at the same time as the connective-tissue cells in the intima and of the adventitia had proliferated, the result being a thick ring around a wide lumen. In the dense infiltration were many larger and smaller multinucleated giant cells. There was no marked necrosis. In many places the process extended throughout the whole segment of the vessel, but in other places the segment was only partially involved. Smaller arteries might be practically closed and in the remnant of the lumen thrombi were present. Among the epithelioid cells were lymphocytes and also different

kinds of plasma cells as well as yellow iron-containing pigments in amorphous masses or enclosed in larger cells. In the central ganglia there was the same picture with in places pure hemorrhages. The lumen of the arteries might be filled with epithelioid and giant cells, the process being perhaps more intense here than elsewhere, usually focal but also more diffuse throughout the arterial walls as well as beyond. The cells were mostly mononuclear, but there

FIG. 3.—The vein (below to the right) shows some inflammation, but the two arteries are extensively infiltrated and there is proliferation, especially in the intima of one of them; in the other the lumen is closed and there are two giant cells among the epithelioid cells; some necrosis in the media.

were also plasma cells and polymorphonuclear leukocytes, sometimes in large masses. There were no necrotic foci, but in the neighborhood of the severely involved vessels the ganglia cells showed degeneration in varying degrees.

No microbes could be demonstrated in the sections (Loeffler's method, Gram's method, stains for the tubercle bacillus and Levaditi's method for spirochetes).

In this case we have a chronic cerebral disease in a woman, aged

twenty-six years, of uncertain nature, so that no definite clinical diagnosis could be made, although the manifestations clearly pointed more and more to organic brain lesion. To the naked eye the appearances in the brain were also puzzling, their being no definite meningitis, the most striking feature in the brain substance being larger and smaller hemorrhages and infiltrations both on the surface and in the deeper parts. The microscopic examination demonstrated a diffuse and marked inflammatory process connected especially with the arteries, the essential lesion being arteritis, but of what kind? It would seem that the anatomical picture does not correspond to that of any known disease. Lethargic encephalitis is different both as to localization and the kind of inflammatory process, especially in that in this disease it does not concern a primary arterial affection. And then the clinical picture does not correspond to that of lethargic encephalitis. Cerebral syphilis must be considered: Spirochetes were not found, and it is noteworthy that the anatomical lesions differ from those of syphilis. The history does not indicate syphilis (Wassermann's test was negative). There were no gummatous changes. Syphilitic endarteritis, as a rule, does not appear as a diffuse process being generally confined to the larger branches, particularly at the base, and to limited vascular areas, being accompanied generally with thrombosis and narrowing, so that necrosis and softening of the corresponding parts of the brain take place. The hyperemia, the dilatation and infiltration of the veins and the multiple hemorrhages do not correspond to the usual picture of syphilis of the cerebral vessels. The absence of necrosis and caseation speak against syphilis while the marked proliferation of the intima with formation of giant cells remind one somewhat of syphilitic endarteritis. At the same time the intima did not show the marked proliferation usually found in syphilis and, on the other hand, the media was more torn apart than is usual in syphilis. The possibility of syphilis may not be excluded, but the entire clinical picture, together with the anatomical lesions, must be said to go against syphilis.

In periarteritis nodosa the clinical phenomena are variable. Practically all organs may become involved. The duration in this case is longer than seen in periarteritis nodosa, but of course that does not exclude it. It is more important to note that the cerebral arteries are rarely involved in periarteritis nodosa, only two cases being described in the literature. Chovstek and Wechselbaum[10] in 1877 described a case in a soldier, aged twenty-three years, who died after seven months of illness with marked cerebral symptoms and in whom the principal cerebral arteries showed multiple aneurysms. And Müller[10] records a similar observation in a man, aged thirty-two years, who was ill for six or seven months with cerebral

[10] Müller, P., Festschr. z. Feier d. 50 jährigen Bestehen der Stadtkrankrah., Dresden-Friedrichsstadt, 1899.

and ocular symptoms. To the naked eye there were only scattered hemorrhages of the brain, but microscopically there was inflammatory infiltration in the walls of the vessels with narrowing of the lumen and necrosis and hyaline degeneration of the walls; the arteries in other organs were involved in the usual manner. None of these cases, however, resemble the one I have described when close comparison is made. Furthermore, there were no nodules or aneurysms in my case. The marked thickening and necrosis in the media, which is so characteristic of periarteritis nodosa, being regarded by many as the primary anatomical lesion, was absent in my case.

While neither syphilis nor periarteritis nodosa, as a rule, does not show the anatomical lesions described in this case, they may hardly be definitely excluded, especially not syphilitic endarteritis.

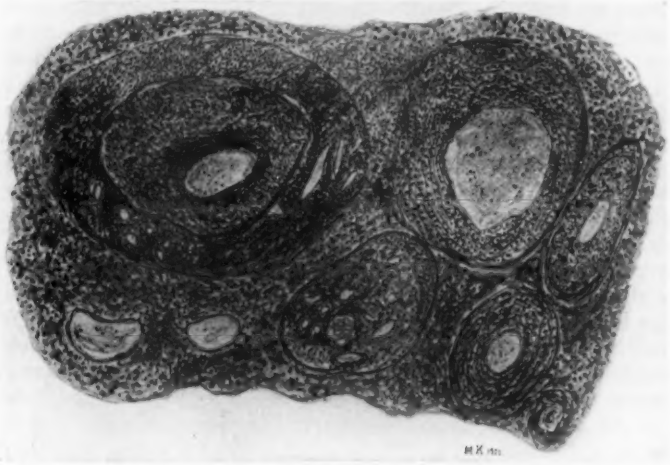

FIG. 4.—Extensive inflammatory changes in small veins and arteries in the bottom of a sulcus, with narrowing and closure of the lumen.

CASE IV.—*Cerebral Arteritis with Mental Disturbances* (Figs. 4 to 6). A sailor, aged forty-six years, was placed in an insane hospital (Dr. Platou) in January, 1919, on account of confusion and hallucinations. He made peculiar movements, *e. g.*, swimming movements, both when standing and when lying down, and would have attacks of violence for a day or so followed by periods of mental clearness, and in the latter part of March he was discharged as cured. It was thought that alcoholism was at the bottom of his trouble.

In June he began to suffer from attacks of fainting, dizziness, vomiting, and later of impulsive violence, when he wanted to kill

his sister, and in August he was again confined. He was restless and talked a great deal of nonsense; the right pupil was larger than

FIG. 5.—All layers of arterial branch extensively involved.

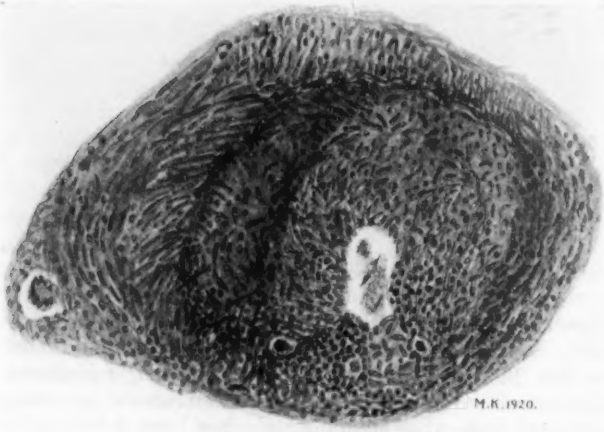

FIG. 6.—Note giant cells and extensive infiltration.

the left, but reacted to light and accommodation; a little later the left face seemed to be paralyzed. He had had chancre in 1904, but the Wassermann was negative. In the middle of September he

was completely disoriented, could hardly walk and was soporous. Death on September 30.

No definite diagnosis was made, but it was thought that the psychosis depended on an organic brain disease.

The postmortem showed no special changes in the heart or arteries; mucopurulent bronchitis in the right lung; liver and kidneys normal; no special changes in the lower urinary tract or in the digestive organs; no tuberculosis anywhere.

The dura showed a growth as large as a hazelnut extending inward into the brain in gyrus centr. ant. sin. The pia arachnoid was thick and adherent. In the upper part of the left temporal lobe was a soft mass including a nodule as large as a walnut; there were several growths of hazelnut size in both hemispheres, of firm consistency; no sclerosis in the vessels; ventricles not dilated.

Some of the growths were subjected to careful microscopical examination. It was found that vessels extended into the center of the growths; the vessels were thick and the lumen narrowed, in places thrombotic. There were no tubercles or larger caseous or gummatous infiltrations as are characteristic of syphilitic meningo-encephalitis. It concerned an inflammatory process concentrated about and proceeding from the bloodvessels and extending into the brain substance, which was edematous and hyperemic, with dilated vessels, and an inflammatory infiltration extended outward into the brain substance from the affected vessels. It was characteristic that these infiltrations all involved the surface of the brain, or rather the pia arachnoid, from which the process extended into the brain. The process may be described more minutely as follows: From the surface of the brain the infiltration would pass down between two gyri, increase in thickness so that it would form a mass in the bottom of the sulcus and extend into the substance along the vessels; in the center would be recognized the contour or remnants of several larger vessels, completely obliterated, in a partly necrotic, extremely cellular tissue, smaller infiltrations extending farther along widened vessels with infiltrated walls. The infiltration consisted of rather large mononuclear cells, lymphocytes, plasma cells, eosinophile cells, but, as a rule, without any polymorphonuclear leukocytes, but in places would be cells with fat granules. Extending into the brain substance the infiltration was principally perivascular, consisting mostly of mononuclear cells. The most striking feature was the involvement of the medium-sized arteries in the sulci and of their branches into the brain, the veins being also involved but in less degree. All the coats of the arteries were thickened and infiltrated, the intima being so greatly thickened that the lumen might be completely obliterated. This change of the intima seemed to be due largely to proliferation of its connective-tissue elements, less to invasion of other cells. In some of the smaller arteries were found multinuclear giant cells, rather small,

the nuclei partly central, partly peripheral, partly diffusely scattered over the cells, which occurred especially in the peripheral layer, and intima. In the most severe lesions the different layers of the arteries would disappear, leaving only the outlines of the vessels in the midst of necrotic granular material, but nowhere was there any arrangement like that in tuberculosis or definitely caseous foci. The involvement of the veins was less marked; in places the veins were thrombotic, and in larger necrotic areas they were also necrotic. Surrounding larger masses the small vessels of the brain were greatly dilated and congested.

It would seem that the brain lesion described in this case was the cause of the mental disturbances during life. It is more reasonable to take this view than to believe that in addition to the changes described there had existed also a separate and distinct mental disease. But the principal question is, What kind of arterial disease was this? The first thought was that it concerned a tuberculous process. The vascular infiltrations with the numerous giant and epithelioid cells might point in this direction, but real tubercles or typical tuberculous granulation tissue was not found and tubercle bacilli could not be demonstrated, nor was there any tuberculosis in other organs, hence we are forced to conclude that it does not concern a tuberculous process. Lethargic encephalitis is contraindicated both by the clinical symptoms, the localization and character of the lesions. In fact, no changes such as have been observed in the various stages of this disease were found in the case under consideration. The possibility of syphilis must be considered. There is the history of chancre in 1905; it is true that the Wassermann reaction of the blood serum was negative, but this of itself hardly excludes syphilis. The absence of syphilitic changes elsewhere do not necessarily exclude syphilis. The vascular process resembles in many ways syphilitic arteritis; proliferation of the intima resembles the syphilitic, although perhaps not so marked; the cellular infiltration in the other vascular coats also remind one of syphilis; and numerous giant cells do not exclude syphilis, although they are more numerous here than usual. Against syphilis we have the marked thickening and necrosis of the media and adventitia and the disintegration and destruction in places of the elastic tissue in the media. Spirochetes were not found, but it is difficult indeed to demonstrate spirochetes even in definitely syphilitic vascular processes. The localization is not inconsistent with syphilis, but a widespread process is rare in syphilis, and it would be expected that gummatous and caseous foci would be found in case it concerned syphilis, but they were absent. We see that while important arguments may be brought forward against syphilis it cannot be definitely excluded.

The localization speaks against periarteritis nodosa. With the exception of the cases described by Chvostek and Weikselbaum

and Müller,[10] practically all descriptions of this disease state that the arteries of the brain are not involved. However, the lesion itself corresponds quite closely to that of periarteritis nodosa, the extensive necrosis of the media with separation and destruction of the elastic tissue being marked, but in many cases the necrosis was even more extensive than usual in periarteritis nodosa, and giant cells, which were very numerous in this case, are found only rarely in this disease, the principal changes of which, after a duration of say nine months, appear to be proliferation of the intima and media with necrosis and degeneration, with but little cellular infiltration in the vessel wall and no giant-cell formation (Gruber,[11] Abramof[12] and v. Haun;[13] see also my Case VII). In no case was there such marked necrosis as in my Case IV, and no giant cells, but numerous epithelioid cells. It remains to point out that there were no definite or typical aneurysms in this case. Taking everything into consideration it must be acknowledged that in many ways this case reminds one of periarteritis nodosa, but even more of syphilitic endarteritis.

For purpose of comparison I shall now describe a case of cerebral syphilis with vascular changes of a peculiar character and of special interest in this connection.

Case V.—A man, aged forty-two years. According to Dr. S. Höyer he began to have pain in the left ear in July, 1900, and in September a discharge appeared from the ear and a little later the left side of the face appeared to be paralyzed. In October there was found suppurative otitis with a large defect in the membrane, but no tenderness over the mastoid. The forehead could be wrinkled but the left eye closed only slowly and incompletely. By the latter part of December the discharge ceased and the general condition was good. In February, 1901, he suffered some kind of injury, and headache and dizziness came on, together with increased discharge again from the ear. A few days later he became paralyzed suddenly in the right arm and the right lower extremity. In the latter part of March the paralysis was improved, but he seemed dull and complained of pain in the left side of the back of the head and also of dizziness. No choked disk. Radial artery thick and second aortic sound accentuated; pulse 80, unequal; left side of face smooth, no function of facial nerve; left lower extremity immovable; lively reflexes; both arms moved freely, grip strong, tremor; headache, frontal and occipital, drowsiness; external otitis (left). March 29 a complete mastoid resection was made, but nothing abnormal was found, and punctures of the brain did not reveal any pus. The patient became comatose after the operation and died two days later.

[11] Centralbl. f. Herz. u. Gesfasskrankh., 1917, No. 9.
[12] Ziegler's Beiträge, 1899, No. 26. [13] Virchow's Arch., 1920, No. 227.

At the postmortem the tibiæ were found to be thick, the skin scarred and brown; on the inner side grayish-red subperiosteal granulation tissue in small holes in the surface of the bones, otherwise is hard and thick. Skin and skeleton elsewhere showed nothing abnormal.

The heart was a little large, the aorta presented a few small yellowish spots and a small scar between the arch and the descending part.

There was bronchitis and double bronchopneumonia; bronchial nodes calcareous.

Spleen weighed 220 grams; adherent to diaphragm. Liver normal. Kidneys showed some fatty change; bladder normal; right testicle fibrous throughout and contains a yellowish-white, putty-like mass as large as a pea; in the left testicle is a yellowish-white cord containing a small concretion. Digestive tract normal.

In the left temporal fossa was a reddish-brown exudate, and under the left side of the cerebellum. The right hemisphere seemed strongly injected, reddish, while the left was pale. Along the left Sylvian artery and its branches were small yellowish-white or yellowish-gray fibrous lines and spots. Pia arachnoid adherent over the right frontal lobe; the cortex here was peculiarly reddish violet in color. Pia arachnoid over the left hemisphere was free.

The vessels at the base were greatly changed, irregularly thickened and dilated and grayish-red in color. These changes were most marked in basilar artery and in Sylvian arteries, which on the left side showed thrombosis.

Nothing abnormal was found in the left hemisphere except a small softened focus between the caudate nucleus and the internal capsule and a little larger focus in the outer part of the lenticular nucleus. The right hemisphere was hyperemic and free from other changes. There was a thin veil-like layer around the medulla and the upper part of the cord; cord and its membranes otherwise normal.

Diagnosis. Syphilitic endarteritis of the cerebral arteries with thrombosis in the left Sylvian artery, softening in the left caudate and lenticular nucleus; meningo-encephalitis over the right frontal lobe, the left temporal lobe and medulla; hyperemia of the right hemisphere; fibrous and caseous syphilitic orchitis; syphilitic periostitis of the tibiæ; bronchitis and bronchopneumonia.

Microscopically the walls of the arteries showed an extensive, somewhat irregularly distributed, even purely nodular inflammatory process, often with great narrowing of the lumen. The adventitia was always the seat of an extensive round-cell infiltration and also in places of connective-tissue proliferation. The media showed degeneration of the muscle cells and of the elastic layer which were broken especially the internal elastic layer underneath foci in the intima containing giant cells. The intima showed the greatest

changes: the cells had proliferated and formed compact masses which narrowed the lumen and even formed swellings of the wall. In places there was complete obliteration, oftenest due to secondary thrombosis. Giant cells, single and in masses, with peripheral nuclei and a degenerated center were found oftenest in the peripheral part of the intimal proliferation, sometimes forming tubercle-like nodules or miliary gummas. There were also foci with a great number of giant cells. A characteristic feature was numerous newly formed small vessels in the intima, and it seemed as if certain necrotic foci were due to obliteration of small vessels.

Besides the lesion in the arteries there were inflammatory changes in the membranes, more over the right hemisphere than the left, and most at the base, but present also over the medulla and the dorsal cord. The infiltration consisted of lymphocytes and some plasma cells and was directly connected with the changes in the adventitia, being often very marked around small arteries as well as veins, along which the infiltration extended into the cortex, which especially on the right side was quite hyperemic. On the inner side of the dura over the left temporal lobe was round-cell infiltration as well as fresh exudate.

This case is interesting first because of the difficulty in the way of a clinical diagnosis and next because of the extent and nature of the lesions in the brain, leptomeningeal and vascular. The endarteritis is remarkable because it occurred in the form of nodules in the region of the left Sylvian artery that often looked like aneurysms and reminded one of periarteritis nodosa. However, taking the case as a whole, there can be no question that it concerned syphilis.

The numerous giant cells in the granulation tissue in the walls of the smaller arteries with degeneration in the intima and media place this case in a rather unusual group of gummous endarteritis. Otherwise the endarteritis seems to correspond to the usual descriptions. It is true that formerly it was denied that giant cells occur in syphilitic vasculitis, but Wright[14] and others have shown conclusively that they may occur.

The microscopic picture excludes periarteritis nodosa, but it brings to mind the tuberculous form of vascular lesion, but no tubercle bacilli were found—there were no tuberculous processes anywhere else—and inoculations of guinea-pigs with the caseous material from the testicle had no effect.

CASE VI.—*Syphilitic Coronary Arteritis Resembling Tuberculosis* (Figs. 7 to 9). Some years ago I[15] studied a case of gummous syphilis of the heart in a man, aged thirty-eight years, who had had syphilis fourteen years before and who was sick for four days

[14] Report of the Massachusetts General Hospital, 1909.
[15] Norsk. magasin f. Lägevidenskabeen, 1914.

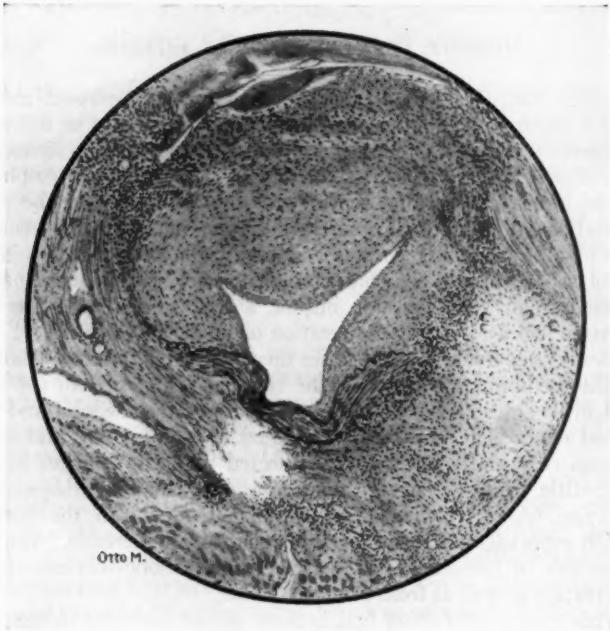

FIG. 7.—Extensive syphilitic endarteritis with necrosis and giant cells.

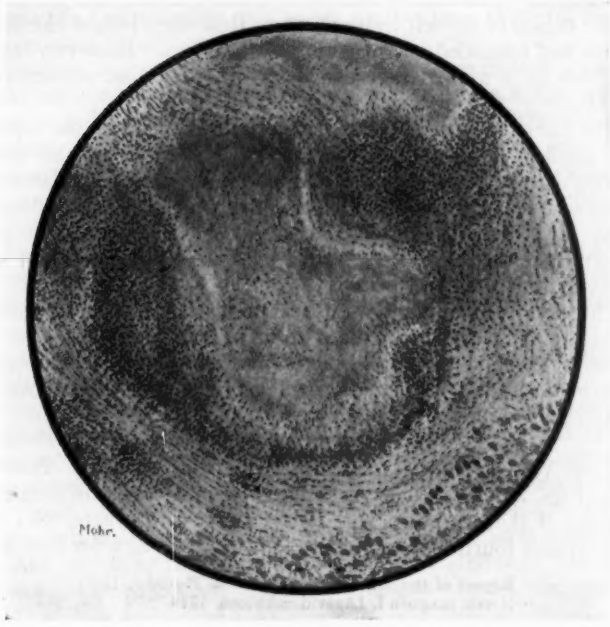

FIG. 8.—Gummatous area in the heart wall with necrosis in the center.

with dyspnea, cyanosis and rapid pulse. Gummas were found, particularly in the walls of the right ventricle and the atrium, which had resulted in obliteration of the superior vena cava. There was also a syphilitic endarteritis in the coronaries and a circumscribed gummous process in the pleura and adjacent parts of the left lung. In this case the changes in the walls of the vessels—necrosis, giant cells, etc.—resembled greatly tuberculosis, as shown by Figs. 7 to 9.[16]

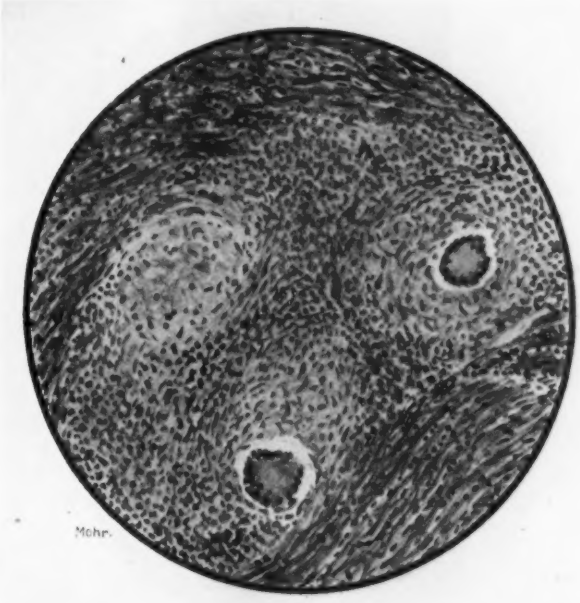

FIG. 9.—Inflammatory gummatous process in the heart wall; epithelioid cells and giant cells. The appearance in Figs. 7, 8, and 9 resemble tuberculosis.

Finally, I wish to give a brief summary of a typical case of periarteritis nodosa.[17]

[16] In Norway it was early pointed out that syphilis may be the cause of important diseases in the internal organs, particularly the brain, the heart and the kidneys. Thus Gjör in 1857 described thirty cases of cerebral syphilis early in life, including cases of apoplexy, hemoplegia and general paralysis. Furthermore, E. Winge in 1863 described changes in the internal organs in syphilitics, including a case of gummous aortitis and gummas in the heart with aortic aneurysm and a case of gummous spinal pachymeningitis. But it was particularly G. Heiberg who insisted on the importance of syphilis in vascular diseases; he demonstrated in the medical society in Christiania (see Transactions, 1876, 1877, 1886) numerous specimens of syphilitic arteritis and aneurysms.

[17] Ibid., 1917.

CASE VII.—*Periarteritis Nodosa* (Figs. 10 to 14). The patient was a man, aged twenty-two years, who began to suffer with stabbing pains in the left foot in April, 1916. Later he noticed that the left foot, which was tender, felt dead. It was easy for him to stumble. In the middle of May similar pains appeared in the right foot and leg and the condition in both feet became worse, at the same time as he had some fever. There was nothing of interest in the family history and the patient himself had never been seriously ill; no syphilitic infection. The cerebral nerves and the upper extremities

FIG. 10.—Heart from the left side with numerous nodules on the small arteries.

were not involved. The lower extremities were normal in position, rather thin, no tremor, no rigidity, rather weak. The muscles in the legs and thigh were tender. The walk was somewhat paretic and he could not walk on his toes or sit on his feet. Wassermann reaction negative. In November palpitation of the heart appeared; the pulse was frequent with a pressure of 160; later dyspnea appeared also systolic murmur. The urine contained albumin and casts. There was also tenderness in the epigastrium with vomiting and a slight icterus. In December edema appeared about the ankles and scrotum, also diarrhea, and the dyspnea increased, there being also

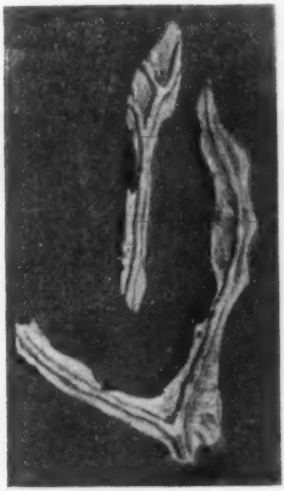

FIG. 11.—Arteries from the omentum with numerous small nodules.

FIG. 12.—Cross-section of the coronary branch, showing infiltration of the intima with calcareous deposit, partial destruction of the media and infiltration of adventitia.

cough with bloody expectoration. The edema increased, ascites developed, the vomiting became worse and the vomited matter contained blood. Death occurred in January, 1917.

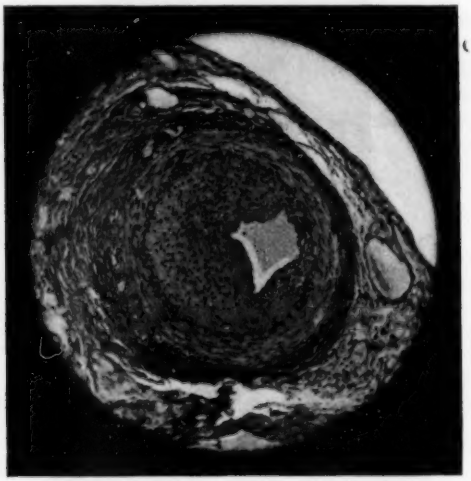

FIG. 13.—Photomicrograph of the artery in the omentum. × 150.

FIG. 14.—Photomicrograph of the arterial branch in the muscle of the leg. × 70.

The postmortem examination showed altogether normal conditions in the brain and its membranes; the arteries at the base showed no changes.

The heart with 570 grams, and as shown in Fig. 10, the coronaries, which were very prominent, showed here and there oval grayish-white nodules up to the size of a hempseed, most numerous along the left side and posteriorly. In the muscles were peculiar yellowish-white spots and stripes as well as hemorrhagic infiltration, and also fibrous streaks. The heart valves were normal.

Lungs and pulmonary arteries were normal; hydrothorax. The organs of the neck and mouth were normal.

There was some ascites. The spleen contained an anemic infarct and three or four small yellowish-white spots. The liver weighed 1040 grams, fatty and passively congested. The vessels on the surface appear as white, thick strings, especially marked on the anterior surface of the right lobe.

The kidneys weighed 310 grams; on the surface numerous irregularly distributed bluish-red, slightly depressed infarct-like areas; on the surface the vessels were more prominent than usual and thicker; on the border between the cortex and the medulla are some grayish-white nodular prominences.

Adrenals and pancreas normal.

On the surface of the stomach the arteries are distinct and here and there are pinhead-sized nodules on the smaller branches. In the mucosa of the smaller curvature near the pylorus is a small ulcer and near it is a small nodule on a little arterial branch. There is a hemorrhagic erosion in the fundus. In the ileum the membrane is hemorrhagic, the follicles prominent; the large intestine showed a swollen lining with hemorrhagic infiltration and necrosis here and there.

The arteries in the omentum are nodular throughout.

The aorta is a little uneven and thick along the posterior wall; this is also true of the iliacs, but the large abdominal arteries are normal.

The spinal cord seems normal, also the vagus, phrenic, brachial, ulnar and sciatic nerves, but there was some edema and small hemorrhages in the connective tissue and muscles about the latter three nerves.

The microscopic examination of the smaller arteries in the omentum, the stomach, the heart, the kidneys and the spleen showed marked swelling of the media and intima in places, due principally to a hyaline degeneration of the connective tissue, in which were only few fibroblasts and here and there some calcareous infiltration. The change was most marked in the intima. In the media the muscle fibers and elastic layers were degenerated but not necessarily all around the lumen. The thickening led to narrowing and even complete obliteration of the lumen and also irregular nodules, so-called aneurysms, which were solid. These changes were most marked in the arteries of the heart and kidneys. In the adventitia there were only slight cellular infiltrations. Similar changes were

found in the small branches of the popliteal, in the branches of the brachial plexus and in the median and sciatic nerves with surrounding muscle tissue, and in this case there was also considerable infiltration in the connective tissue around the arteries and in the nerves, mostly of lymphocytes.

In the heart muscles was infiltration of the lymphocytes, increased in fibrous tissue, and degeneration with fragmentation of the muscle fibers with calcareous dust in places. In the kidneys degenerative and inflammatory changes as well as infarcts were present in addition to the arterial changes.

In the other organs there were no special microscopic changes other than those indicated by the naked-eye examination.

Summarizing the changes it may be noted that the smaller arteries in the heart, the kidneys, the stomach, the intestine, the omentum and in certain muscles and nerves were the seat of a productive inflammatory process, particularly in the media and intima; in the arteries in the muscles and nerves there was also an exudative process, particularly in the adventitia.

Periarteritis nodosa presents different clinical forms according as different organs are involved. It begins usually acutely in previously well persons and attacks mostly young and strong men between twenty and forty years of age, the first symptoms as in this case being indefinite pains in the muscles of the trunk as well as of the extremities and in the joints with fever; there may be edema and changes in the skin with disturbances in sensibility, paresis, exhaustion and weakness, the pulse often being very frequent and irregular. Death usually occurs after some weeks up to six or eight months after increasing weakness, dyspnea, renal and digestive disturbances as well as cardiac troubles. Death has been observed as early as ten days from the beginning and as late as after one or two years. The most common form is the muscle-nerve type, to which the case I have described belongs. In other cases the principal symptom may be renal or gastro-intestinal or cardiac; other organs, *e. g.*, the skin, may be especially involved, but as before stated the brain is rarely affected. The disease appears to be curable —four such cases have been described—and it may well be that more instances of recovery of mild or abortive forms will be recognized as the disease becomes better known. Most of the cases—between sixty and seventy in all—have been described in German literature and only remarkably few in the English and American.

The primary anatomical changes are in the small and medium-sized arteries in the heart, kidneys, digestive tract, etc., where they give rise to the very characteristic oval grayish-white, usually firm aneurysm-like nodules in linear arrangement on the small arteries. The lumen is usually narrowed, but true aneurysms have been observed. The large arteries, as a rule, are not involved. The narrowing and thrombosis of the arteries form the basis for the

other anatomical changes as well as the clinical phenomena; necroses and degenerations, hemorrhages and hemorrhagic infiltrations.

Microscopically the inflammatory changes in the arteries appear to be infectious. There is no agreement as to whether the changes develop first in the media or adventitia, although many believe that the media is first involved, fibrinous exudation and edema with degenerative and necrotic changes in the muscles fibers and elastic tissue, together with round-cell infiltration preceding the formation of connective tissue. By some the primary lesion is believed to be a periarteritis which extends into the media and involves the intima in proliferation. When the changes are acute true aneurysms may form.

Such in brief appears this disease of the arteries. It has many things in common with the so-called syphilitic endarteritis, but there are also differences. As emphasized by Guldner,[18] the presence of spirochete and a positive Wassermann reaction would establish the diagnosis of syphilis, which frequently involves the cerebral arteries while periarteritis nodosa rarely occurs in the brain; in syphilis the intima is first involved, whereas in periarteritis the media or the adventitia; in syphilis gummatous changes and giant-cell formation occur while the latter is rare in periarteritis nodosa; and finally in the syphilitic endarteritis the elastic membranes are split apart and new elastic tissue may be formed, but there is no such fracturing of the elastic layers as in periarteritis. Spiro[19] points out that the infiltration in periarteritis regularly contains polymorphonuclear leukocytes, which are absent in syphilitic endarteritis, and the vessel wall is attacked only partially in periarteritis, whereas in syphilis the process usually extends all around the vessel. It should be noted that in syphilitic endarteritis the intima may be attacked secondarily; that the giant-cell formation is rather unusual in both these forms of arterial disease, although more so in periarteritis nodosa; and the necrosis in periarteritis nodosa may be quite considerable even though large gummatoûs areas do not form. There seems to be no absolutely distinctive difference between these two diseases of the arteries, and consequently it is not difficult to understand that they may be confused. Versé[20] has advanced the opinion that they may be identical because they have so many things in common; thus aneurysms may develop in syphilitic endarteritis and necroses are present in both processes as well as giant-cell formation, and he suggests that periarteritis nodosa may be a special form of arterial syphilis affecting small and medium-sized arteries—but if only a few of the cases of periarteritis nodosa has syphilitic infection been definitely demonstrated and, as a rule there is no history of syphilis and the Wassermann

[18] Virchow's Arch., 1915, No. 219.
[19] Ibid., 1920, No. 227.
[20] Ziegler's Beiträge, 1907, No. 40.

reaction is negative. While it is true that the lesions in these two diseases in many respects corresponds in particular details, the complete anatomical picture seems to me to indicate that it concerns two distinct diseases.

Certain writers hold that periarteritis nodosa is not a distinct entity because no specific virus as yet has been demonstrated and because various pyogenic microbes have been found in some of the cases (staphylococci, streptococci;) it is also pointed out that preceding infections such as angina, typhoid fever, diphtheria and acute rheumatism may be regarded as predisposing, in some cases at least, to the development of periarteritis nodosa. It is true, as discussed in the earlier part of this article, that arteritis occurs in different forms of infection, but at present the view that the disease is not specific may be regarded as merely hypothetical. To me it seems most reasonable to regard periarteritis nodosa as a definite disease due to a distinct virus. While the clinical picture may be variable, depending on the distribution of the lesions of the arteries, the lesion itself is quite characteristic enough to warrant the belief that it concerns a specific disease. Recently, v. Haun[21] by inoculation of the blood of a patient with periarteritis nodosa claims to have produced the disease in guinea-pigs, but of course further investigation is required.

In conclusion I would point out that forms of true arteritis occur more frequently than usually believed, that they apparently differ etiologically, and that they present anatomical appearances that make the differential diagnosis difficult, this being particularly true of the vascular changes in syphilis, periarteritis nodosa and also in tuberculosis.

POSTOPERATIVE DIETOTHERAPY.[1]

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Prior to the middle of the nineteenth century the dietetic treatment of most acute disease conditions consisted in virtual starvation. Graves, in 1848, first insisted that a fever patient should be fed. Today clinicians are in accord regarding the dietary treatment of febrile conditions. The high calorie treatment of typhoid fever is a

[21] Virchow's Arch., 1920, No. 227.

[1] Read before the Richmond Academy of Medicine, Richmond, Va., February 22, 1921.

more recent development, but its value has been demonstrated beyond cavil. Many a case so treated has on convalescence weighed as much as he had before the onset of his illness, and the frequency of complications has been diminished. In the treatment of lobar pneumonia little attention was formerly paid to dietary regimen. This is a limited disease, usually of one week or of ten days' duration. Physicians believed that for this period the patient could do well on any diet, provided it was light enough, and as a result it usually consisted in liquids of low food value. But pneumonia often, by developing complications, becomes a protracted disease. In this case the diet becomes most important, and those individuals who have been practically starved throughout the first week must continue the fight at a handicap. In the more modern treatment every pneumonia patient is considered as potentially a chronic, wasting case.

The surgeon notoriously pays less attention to dietary treatment than does the internist. In many surgical clinics postoperative treatment still consists in partial starvation. The desire to prevent nausea and vomiting results in undue caution. We do not imply that an individual whose stomach is upset should be fed, but would emphasize that food should not be withheld for several days after the acute gastric symptoms have subsided. A certain number of surgical cases develop complications requiring prolonged treatment. Just as in pneumonia it is essential that every case be treated as potentially of long duration. No harm will be done to those who recover rapidly, and the precaution may be life-saving to those who are so unfortunate as to develop untoward sequelæ.

It is our intention to discuss in this paper only the general dietary management of postoperative cases without reference to those instances in which the presence of complicating medical conditions or operations on digestive organs call for special methods. The latter group is of great importance and merits intensive discussion, but time permits reference only to general dietary principles in surgery.

The treatment of operative cases begins before operation. It is frequently advisable to keep the patient in bed for some days prior to operation, in order to build up the general resistance. A light, highly nourishing diet relatively rich in carbohydrates may be given up through the day preceding operation.

The importance of a liberal fluid intake before operation cannot be overemphasized. Recent studies in the causation of shock bring out the important role played by the fluid content of the blood. The symptoms of shock are due to a deficient amount of circulating fluid in the bloodvessels. In midly shocked individuals this deficiency follows a draining of blood into abnormally dilated capillary beds, while in severe shock there is added a loss of fluid by transudation out of the vessels into the tissues, due to an abnormal per-

meability of damaged capillary endothelium. The prevention of shock depends in part at least on the maintenance of a normal blood volume. The practice still occasionally in vogue of withholding fluids for some hours previous to operation results in preliminary dehydration and renders the body less able to combat shock when it occurs.

Following operation the patient usually receives nothing by mouth during the first twenty-four hours. During this period the stomach is usually upset and there is a strong tendency to nausea and vomiting. If these symptoms are absent there is no reason for protracted withholding of food. The administration of fairly abundant fluids before operation frequently lessens the tendency to nausea and vomiting. Another precautuon which is frequently successful is that of washing out the stomach while the patient is still under the influence of the anesthetic. As soon as the stomach will tolerate ingested material fluids may be administered. It is best first to try out the patient with water or with weak tea, or if stimulation is necessary, strong coffee. Usually by the second day the patient is in condition to take liquid nourishment. Sometimes this occurs sooner.

The liquid dietary used in most surgical clinics, and also in many even of the more progressive medical clinics, is based upon two essential food substances: milk and raw eggs in the form of egg-white, albumen water or eggnog. Milk is frequently contraindicated in postoperative conditions because of the tendency to distention, and therefore albumen water is often the chief constituent of liquid diets. Scarcely any food substance is less fitted to be the principal article of diet than is uncooked egg-white.

The popularity of this article in treatment arose from the classical work of Beaumont, who found that raw egg-white left the stomach more rapidly than did any other food, and concluded that it was more rapidly digested. Little attention has been paid to more recent work demonstrating that this rapid emptying occurs because raw egg-white is not digested at all in the stomach.

Bateman has summarized the evidence in support of this statement. The outstanding facts are as follows: Raw egg-white has but feeble ability to stimulate the flow of gastric juice. It is actually no more powerful than a similar amount of water. Cooked egg-white, on the contrary, causes the production of an abundant gastric secretion and unites rapidly with the hydrochloric acid. The raw untreated substance possesses an antibody which resists the action of pepsin. Not only is it resistant to digestion in the stomach, but it has also an antitryptic action. It calls forth no increased secretion of bile. After having passed the stomach it is but poorly digested in the intestines. Native egg-white when fed with other easily digestible proteins prevents the digestion and absorption of the latter. This has been proved by numerous investigators. Bate-

man suggests as an explanation that the colloidal egg-white absorbs the trypsin, thus diminishing its activity in much the same way as does charcoal.

Administered by mouth, raw egg-white produces diarrhea and sometimes vomiting in dogs. This has been produced by as small an amount as the whites of two eggs. Diarrhea has also been produced in numerous cases in man even after as small a quantity as the whites of four eggs. Mendel and Louis have shown that after the ingestion of small amounts of native egg-white the latter could be recovered unchanged from the stools. In experimental work it made little difference whether the raw food was eaten alone or with other foods. In the latter case diarrhea was later in appearing. Substances added to the diet which stimulate the flow of gastric juice do not aid in the digestion of egg-white. In man from 30 to 50 per cent of egg-white is completely lost as such in the feces.

Cooked egg-white produces none of these symptoms, and when fed even in large amounts 90 per cent of it is utilized. It is only necessary to produce coagulation. Coagulation is complete with a resultant jelly-like mixture if the temperature is raised to 70°. Heating to a higher point and cooking more thoroughly in no way impairs the digestibility.

Experiments on man consisting of the feeding of raw egg or egg-white produced, as a rule, either diarrhea or flatulence, or both. This sometimes occurred with as small an amount as the whites of four eggs daily. The beating of eggs into a froth made little difference in the result.

Hamburger and Cramer claim that albuminuria follows the ingestion by man of large amounts of beaten egg-white. Stokvis believes that raw egg-white taken in quantity is absorbed and undigested and excreted in the urine, thereby damaging the renal epithelium. Quite recently Van Alstyne has shown that raw egg-white taken into the alimentary tract may enter the circulation and be excreted through the urine.

In spite of the foregoing facts one may find on perusal of current books on dietetics that raw egg-white is still extensively recommended as an excellent nourishing food for invalids.

We may sum up the case against uncooked egg albumen in saying: (1) That it is very poorly digested and absorbed; (2) that as high as 50 per cent is lost in the feces; (3) that it tends to produce gastrointestinal upsets; (4) that at times it appears to produce an albuminuria, a condition certainly not to be desired in postoperative cases in which the kidneys already are overworked, as evidenced by the frequency of albuminuria following general anesthetization. All of these disadvantages are eliminated by the simple process of coagulation.

While egg-white is principally protein the preponderating element in the food of postoperative cases should be carbohydrate. During

operation the metabolism is usually increased and the reserve supply of carbohydrate in the body is to some extent depleted. Carbohydrate should now be administered to furnish additional energy and to protect the patient's own body protein. If protein alone is given the basal metabolism increases as a result of the specific dynamic action of protein. Protein so stimulates the metabolism that the rate of heat formation in the body is accelerated. Sugars and fats have a similar dynamic action, but to a much less marked degree.

Most patients after undergoing an operation and postoperative treatment leave the hospital weighing decidedly less than upon entry. It seems reasonable to hope that under proper dietary care these patients may do equally well as those treated by high calorie, high carbohydrate diets in typhoid fever, and that individuals may leave the hospitals weighing as much as or more than upon entrance. If this is to be attained it can best be done by feeding diets of relatively high caloric value and relatively high in carbohydrates.

It is nevertheless essential that sufficient protein be administered to repair the waste and loss of protein from the body tissues. Chittenden has shown that with slightly less than 1 gram of protein per kilogram of body weight the amino-acid requirements of the tissues will be safely met. The average adult individual weighs about 70 kilograms. With 1 gram of protein necessary per kilogram of body weight the daily diet should then contain approximately 70 grams of protein. This will contribute about 280 calories to the daily requirement, and we must rely upon carbohydrates and fat for the balance. It makes little difference which of these two latter substances preponderates as long as the fat does not furnish more than 90 per cent of the non-protein calories. In view of the tendency to acidosis in postoperative cases, as indicated by the presence of acetone in the urine, it would appear more rational to utilize carbohydrates in preference to fats.

To return to a discussion of the protein it is important to note that recent researches have shown that different proteins vary greatly in their ability to maintain nitrogenous equilibrium. This is because certain ones, such as those from cereals, are deficient in one or more of the essential amino-acids. Van Slyke remarks that a man who might be kept in equilibrium on 4 grams of nitrogen per day in the form of beef, milk or eggs would require 8 grams as bread or potatoes and 16 grams as beans. Thus it would appear advisable when we are giving proteins to give those of higher value, such as meat or meat derivatives, milk, eggs and fish. We must differentiate between proteins of good quality and those of poor quality.

It is not enough that a diet possesses sufficient calories and is composed of the right proportion of foodstuffs. Sufficient vitamines must be present. The food must be palatable. There must be sufficient variation so that the diet will not become irksome. The food must be so prepared that it is easily digested and absorbed.

The physical texture and the fineness of division are factors worthy of consideration. In general the more finely divided the food the more rapidly does the digestive juice penetrate and the more rapidly does digestion take place. Indigestible solids not only act as stimulants to peristalsis but apparently actually retard normal absorption. The method of cooking is important. Fried substances are covered by a layer of material which the gastric juice can neither readily dissolve nor penetrate.

If the diet contains a fairly abundant proportion of milk and of eggs whose albumen has been coagulated there is little danger of deficiency in vitamines, either in the fat-soluble A or in the water-soluble B.

DIET NO. I.—FEEDINGS EVERY TWO HOURS.

Time.		Amount.	Protein, grams.	Fat, grams.	Carbohydrate, grams.	Calories.
7 a.m.	Hot milk	200 cc	6.6	8.0	10.0	138.40
9 a.m.	Oatmeal gruel	100 cc				
	With milk	100 cc	4.5	4.4	11.3	102.80
	Coffee with cream	25 cc				
	With cane sugar	8 gm.	0.55	10.0	8.75	127.2
11 a.m.	Orange juice	50 cc				
	Lemon juice	25 cc				
	Lactose	50 gm.				
	Water	150 cc	0.4	0.1	58.25	235.5
1 p.m.	Chicken broth	150 cc	5.4	0.5	2.25	35.10
	Cocoa	5 gm.				
	With lactose	30 gm.				
	With cream	50 cc				
	With milk	100 cc	5.48	25.44	38.38	404.40
3 p.m.	Buttermilk	200 cc	6.0	1.0	9.58	71.32
5 p.m.	Grape juice	125 cc				
	With lactose	25 gm.	.....	.....	31.25	125.00
7 p.m.	Cream of tomato soup	150 cc	10.65	42.64	41.05	590.56
	Soft-cooked egg	50 gm.	5.95	4.65	.....	65.55
9 p.m.	Hot milk	150 cc	4.95	6.0	7.50	103.80
			50.48	102.93	212.06	1999.73

Time.	From the kitchen.	Amount.	From the floor.	Amount.
7 a.m.	....	.....	Hot milk	1 glass.
9 a.m.	Oatmeal gruel with milk	1 serving		
	Coffee with cream and sugar	1 cup		
11 a.m.	.....	.....	Orangeade with lactose	1 glass.
1 p.m.	Chicken broth	1 bowl		
3 p.m.	.....	.....	Buttermilk	1 glass.
5 p.m.	Cream soup	1 bowl		
	Soft-cooked egg	1 egg		
7 p.m.	.....	.....	Grape juice with lactose.	1 glass.
9 p.m.	.....	.....	Hot milk	1 cup.

Palatability depends (1) on variation and (2) on the type of food administered. Only two food substances are naturally appetizing and do not require seasoning. These are animal foods and fruits. The use of fruit juices for increasing palatability is well known. The addition of meat extracts for the same purpose may be employed.

The accompanying tables are examples of postoperative dietaries in use at St. Elizabeth's Hospital, Richmond, Va. They are made up on a basis of 2000 calories with a protein intake slightly below 1 gram per kilogram of average body weight. It has been amply demonstrated by various workers, and particularly in reports from the Nutrition Laboratory of Copenhagen, that for limited periods

DIET NO. II.—FEEDINGS EVERY TWO HOURS.

Time.		Amount.	Protein, grams.	Fat, grams.	Carbohydrate, grams.	Calories.
7 a.m.	Chicken broth	100 cc	3.6	0.1	1.5	21.30
9 a.m.	Soft-cooked egg	50 gm.	5.95	4.65	....	65.65
	Oatmeal gruel	100 cc	1.2	0.4	6.3	33.60
	Coffee with cream and sugar (cane)	25 cc 8 gm.	0.55	10.0	8.75	127.20
11 a.m.	Grape juice	150 cc	....	....	37.50	150.0
1 p.m.	Cream of green pea soup	200 cc	15.56	56.88	88.04	806.32
	Orange juice	50 cc				
	With lemon juice	25 cc				
	With lactose	50 gm.				
	With water	150 cc	0.4	0.4	58.25	235.80
3 p.m.	Beef juice	100 cc	4.90	0.60	....	25.0
5 p.m.	Malted milk	12 gm.				
	With cocoa	5 gm.				
	With lactose	25 gm.	4.13	4.30	4.01	191.26
	Soft poached egg	50 gm.	5.95	4.65	....	65.65
7 p.m.	Boiled custard	100 gm.	6.27	6.32	31.35	207.36
9 p.m.	Barley water	200 cc	0.52	0.11	3.64	17.63
			49.03	88.11	239.34	1946.47

Time.	From the kitchen.	Amount.	From the floor.	Amount.
7 a.m.	.....	.....	Chicken broth	1 cup.
9 a.m.	Oatmeal gruel	1 serving		
	Soft-cooked egg	1 egg		
	Coffee with sugar and cream	1 cup		
11 a.m.	.....	.....	Grape juice	1 glass.
1 p.m.	Cream soup	1 bowl		
	Orangeade	1 glass		
3 p.m.	.....	.....	Beef juice	1 cup.
5 p.m.	Chocolate malted milk	1 glass		
	Soft poached egg	1 egg		
7 p.m.	Boiled custard	1 cup		
9 p.m	.....	.....	Barley water	1 cup.

of time the reduction of protein intake to as low as 29 grams per day is without deleterious effects. This is particularly true if the proteins are of "good quality" and if the patient is at rest in bed. The caloric intake is slightly in excess of that usually estimated as required by an individual at rest in bed and therefore provides for a slight gain in weight. The diets are all relatively high in carbohydrates.

DIET NO. III.—FEEDINGS EVERY TWO HOURS.

Time.		Amount.	Protein, grams.	Fat, grams	Carbohydrate, grams.	Calories.
7 a.m.	Orange juice	100 cc	0.8	0.2	28.07	117.28
	Lemon juice	15 cc				
	Lactose	15 gm.				
9 a.m.	Cream toast	30 gm.				
	With milk	100 cc				
	With butter	1 oz.				
	With flour	1 oz.	7.78	12.49	7.45	173.33
	Poached egg	50 gm.	5.95	4.65	....	65.65
11 a.m.	Chicken broth	100 cc				
	With cracker	10 gm.	4.58	1.01	8.81	62.65
1 p.m.	Cream of pea soup	200 cc	15.56	56.88	58.04	806.35
3 p.m.	Oatmeal gruel with milk	100 cc	8.72	8.10	21.83	195.10
5 p.m.	Poached egg on toast	20 gm.	7.87	13.39	10.54	194.15
	Butter	10 cc				
7 p.m.	Baked custard	100 gm.	7.60	6.65	12.50	140.25
9 p.m.	Malted milk	12 gm.				
	With cocoa	5 gm.				
	With lactose	25 gm.	10.39	11.56	48.07	237.88
			69.25	114.93	195.93	2092.81

Time.	From the kitchen.	Amount.	From the floor.	Amount.
7 a.m.	.....	.....	Orangeade with lactose	1 glass.
9 a.m.	Cream toast	1 serving		
	Poached egg	1 egg		
11 a.m.	.....	.....	Chicken broth with cracker	1 glass.
1 p.m.	Cream soup	1 bowl		
3 p.m.	Oatmeal gruel with milk	1 serving		
5 p.m.	Poached egg on toast with butter	1 serving		
7 p.m.	Baked custard	1 serving		
9 p.m.	.....	.....	Chocolate malted milk	1 glass.

Diet No. I is usually the first administered and should be given as soon after operation as the patient's condition safely permits. It corresponds to the so-called liquid diet, although there are included in it such non-liquids as strained oatmeal gruel and a

soft-cooked egg. Diet No. II is used interchangebly with the former and is particularly useful in those cases with milk intolerance or with a tendency to abdominal distention. Diet No. III follows Diet No. I or No. II usually by about two days. When it is found that the patient tolerates the first diet well he may rapidly be changed to the third. In this the feedings are alternated, liquid and semisolid. After an additional day or two, or as long as is necessary in each individual case, Diet No. IV is given, consisting of semisolid food.

DIET NO. IV.—FEEDINGS EVERY TWO HOURS.

Time.		Amount.	Protein, grams.	Fat, grams.	Carbo-drate, grams.	Calories.
7 a.m.	Baked apple	120 cc	0.61	0.58	29.30	124.86
9 a.m.	Wheat farina	100 cc				
	With milk	100 cc				
	With lactose	15 gm.	14.50	5.40	96.30	491.0
	Toast with milk	100 cc				
	Toast	40 gm.	7.12	12.54	7.10	169.74
11 a.m.	Plain junket	100 gm.	3.30	4.0	19.67	127.88
1 p.m.	Creamed fish	50 gm.	17.48	18.83	26.24	344.35
	With white sauce	100 cc				
	Purée of spinach	100 gm.	2.10	4.10	2.60	55.70
3 p.m.	Apricot souffle	.....	6.37	21.56	17.85	290.92
5 p.m.	Chicken broth	100 cc				
	With rice	50 gm.	5.0	0.60	1.50	31.40
	Poached egg	50 gm.				
	On toast	20 gm.				
	With butter	10 cc	7.87	13.39	10.54	194.15
7 p.m.	Stewed prunes	100 gm.	0.50	0.10	22.30	92.10
9 p.m.	Barley gruel with milk	120 gm.	5.94	6.41	13.25	134.45
			70.59	87.51	246.65	2056.55

Time.	From the kitchen.	Amount.	From the floor.	Amount.
7 a.m.	Baked apple	1 large		
9 a.m.	Wheat farina with sugar and milk	1 serving		
	Milk toast	1 serving		
11 a.m.	Plain junket	1 cup		
1 p.m.	Creamed fish	1 serving		
	Purée of spinach	1 serving		
3 p.m.	Apricot souffle	1 serving		
5 p.m.	Chicken broth with rice	1 bowl		
87 p.m.	Stewed fruit	1 serving		
9 p.m.	Barley gruel with milk	1 serving		

The feedings in all four diets are administered every two hours. The directions to the nurse are simplified as shown in the accom-

panying tables, which indicate the amount to be given and whether it is to come from the kitchen or is to be made up by the nurse in the ward.

The advantages of these four groups of diets are as follows: (1) A graduated increase in feedings is provided for each uncomplicated case; (2) the diets are composed of the proper proportions of protein, fat and carbohydrate; (3) the nourishing value is high; (4) all diets are sufficiently varied and are palatable.

In practical experience we have found the diets to be satisfactory. No striking advantage over the usual method of feeding is to be seen in the average postoperative case. It is particularly in those cases which develop untoward complications with prolonged convalescence that the comparative advantages become apparent. Nevertheless, we have observed that patients placed on these dietaries are much more content than others treated by the usual method. This paper is in the nature of a preliminary report and will be followed by a comprehensive comparison of the results from the two methods, a comparison of the weight curves and a discussion of the influence on postoperative conditions such as albuminuria and acetonuria.

We would particularly emphasize that in postoperative treatment the diet must be individualized. Every patient is a law unto himself. The patient's likes and dislikes should always be consulted and agreeable food substituted for that which is distasteful. This can easily be arranged in our diet. The dietaries above described will be relished by the majority of individuals, but when necessary substitution should be freely employed provided care is taken not to change the relative proportion of protein, fat and carbohydrate and not to alter markedly the caloric value.

Mendel has said: "Unfortunately, rational dietetics founded upon the newer knowledge of the chemistry of foods and nutrition has not yet received the discriminating study and advocacy on the part of practical clinicians that its importance unquestionably warrants." This paper is a plea for the rational application to practical medicine and surgery of the more recently demonstrated scientific facts in physiology and biochemistry and for the elimination of those principles which have already been proved to be in error.

REFERENCES.

1. Bateman, W. G.: The Use of Raw Eggs in Practical Dietetics, Am. Jour. Med. Sci., 1917, **153**, 841.

2. Friedenwald and Ruhrah: Diet in Health and Disease, W. B. Saunders Company, Philadelphia, 1909.

3. MacLeod, J. J. R.: Physiology and Biochemistry in Modern Medicine, C. V. Mosby, 1919, second edition.

4. McCollum, E. V.: The Part Played in Diet by Food Substances of Unknown Nature, Oxford Medicine, 1920, **1**, 435.

5. Mendel, L. B.: Food Factors in Gastro-enterology, Am. Jour. Med. Sci., 1919, **158**, 297.

6. Van Slyke, D. D.: The Chemistry of the Proteins and their Relation to Disease, Oxford Medicine, 1920, **1**, 251.

ADDISON'S DISEASE: A CASE OF TUBERCULOSIS OF THE ADRENALS.

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The purpose of this paper is to report a case of Addison's disease, including the case history and autopsy findings. The writer is indebted to Dr. J. W. Bruner and Dr. A. C. Morgan for permission to report the case and the use of the clinical report.

During previous experience in postmortem work several cases of Addison's disease have been encountered, two of which stand out prominently. One had been considered a clinical case of Addison's disease and had been used for teaching purposes. At autopsy no lesions whatsoever of the adrenal could be demonstrated. The second case had not been diagnosed and presumably had not shown the clinical features, while at autopsy large tuberculous adrenals were found.

The present case was diagnosed clinically, presenting the classical symptoms, while at autopsy definite tuberculosis of the adrenals was demonstrated. The following clinical history obtained by Dr. Morgan presents the typical signs and symptoms of this disease:

Mr. G. S., aged forty-three years, principal of a high school.

Chief Complaint. October 30, 1920, the patient complained of a very tired feeling which has increased during the past six weeks.

Past Medical History. In November, 1918, he was sick for one week succeeding the influenza epidemic. He has had numerous attacks of tonsillitis until the removal of the tonsils four years ago. Had the usual diseases of childhood. The patient has had an active life working on a farm until twenty-five years old, when he attended the Bloomsburg Normal School and has been teaching ever since. During the summer of 1918, in Maryland, he had an attack of illness of a week in which he complained of being very tired and dizzy, but no pain. He had never had chills, but has been subject to bleeding gums for some time.

Social History. Married for the past eighteen years, but has no children. Wife never pregnant. His heaviest weight was 175 pounds twenty years ago. Average weight, 154 to 164 pounds, and about a month ago this dropped to 151½ pounds. His appetite has been good until the past week. He has been subject to bilious attacks for several years. This has been accompanied by nausea and occasional vomiting lasting for two days. This has occurred

as often as once a week, but lately about every six months. These attacks were relieved by laxatives.

History of Present Illness. The school term of 1919–20 seemed to leave the patient a little more tired than usual. He spent the summer months at Danville, Pa., caring for his father, who died at the age of seventy-seven years. At this time the patient lost considerable sleep and was under great strain. The patient returned to his school duties, and about September 15 noticed that he became extremely tired upon the least exertion. Work seemed to pile up, his strength lessened and he fell back considerably. The patient did not worry over this and had a clerk to aid him. During the past week the weakness seemed to have progressed considerably. The illness is not associated with pain, and walking short distances is accomplished without effort. Standing still causes dizziness and faintness and the patient must sit down to get relief.

Physical Examination. Face and neck are very dark, edging off at the clavicles. At times they are ashen gray. The lips are dusky and pigmented, but not the appearance of cyanosis. The gums are very much pigmented and resemble those of a bull dog. Both nipples show marked deep brown pigmentation, with well-marked lines of demarcation. No pigmentation over the axillæ or pubes. The hands show a tendency to pigmentation, but not to the same extent as does the face. From the wrist to above the elbow the discoloration is apparently due to ordinary exposure effects. The heart outline seems smaller than normal on percussion. No adventitious sounds. The lower border of the stomach is on a level with the umbilicus. The liver is five inches in depth in the right nipple line. The spleen seems increased on percussion in the left axillary line. On deep palpation under the left costal margin there is decided tenderness and apparent resistance down to the level of the umbilicus, but no distinct mass is felt. Bimanual palpation of both flanks gives some tenderness, but without definite localization. The feel of the muscles is very flabby.

Urine Analysis. (*a*) Amber; clear; acid; 1016; negative for albumin, sugar and indican; long, narrow hyaline casts; occasional leukocytes, epithelium and urates.

(*b*) 1020; acid; very faint trace of albumin; indican plus; no acetone, diacetic acid or sugar; urea, 10.56 grams per 960 cc; epithelial cells; hyaline casts (1); bacteria; amorphous urates.

(*c*) 1010; very faint trace of albumin; 1 hyaline and 1 granular cast; epithelial cells and bacteria.

Blood Examination. Red blood cells, 3,840,000; white blood cells, 10,200; hemoglobin, 90, Cl, 1; polynuclears, 45; large lymphocytes, 30; small lymphocytes, 32; eosinophils, 3; microcytes; macrocytes; poikilocytosis. Cells have tremendous ameboid motion. Cannot find malarial parasites in stained specimen.

Blood-pressure. Systolic, 84; diastolic, 58; pulse-pressure, 94; regular tones very soft and without murmur.

Renal Function. December 7, 1920. Reaction time, fifteen and one half minutes. Percentage in first specimen, 15; second, 10; total, 25. CO_2 in alveolar air, 40 per cent.

Blood Examination. December 3. Red blood cells, 3,690,000; white blood cells, 7,200; hemoglobin, 85 per cent; polynuclears, 72; small lymphocytes, 24; large lymphocytes, 2; neutrophils, 2.

Examination of the Chest, Roentgen Ray. Peribronchial markings are well-defined throughout both lungs. The right upper lobe extending from the apex to the first interspace anteriorly shows a definite tuberculous infiltration. The left apex shows a similar condition with several dense small calcified tubercles. The appearance of the condition of the right apex would suggest a more recent activity. Examination of the sinuses show the frontal sinuses quite large, but no evidence of any infection.

Examination of the Teeth. Subject to bleeding gums for some years. Examination shows no evidence of infection of the upper jaw. The lower right anterior bicuspid, which has been crowned, shows a pericementitis with apical infection.

The autopsy was made at the patient's residence through the courtesy of Dr. J. W. Bruner, and the following is the report:

Date of death, January 14, 1921.

Date of autopsy, January 14, 1921, 8 P.M.

Clinical Diagnosis. Addison's disease.

Cause of Death. Bilateral tuberculosis of the adrenals.

Associated Diagnosis. Acute pulmonary hypostatic congestion, bilateral. Cardiac dilatation. Chronic degenerative nephritis with pyramidal anemia. Arrested pulmonary apical tuberculosis.

Gross Description. The body was that of an adult white male, forty-three years of age, moderately well nourished, slight *livor mortis* in the dependent positions and rigor moderately marked eight hours after death. The face and exposed parts of the neck, the hands and lower arms had a dark bronzed color, due apparently to a pigmentation which had diffused and evenly distributed in the cutaneous layer. It was observed that this bronzed color was very much less marked after than before death. The pigmentation did not involve the covered portion of the body, although in these there was a pasty pallor.

The usual primary incision was made from the episternal notch to the symphysis pubis, and the breast plate was removed.

Chest. There was no fluid on either side; the lungs were partially collapsed. At both apices old pleural fibrous adhesions attached the lung to the parietal wall firmly enough on the right side to tear the lung structure during removal.

The right lung, in the uppermost portions, was pallid, soft and crepitant, with moderate lines of anthracotic markings. The dependent position, especially of the lower lobe, was darker blue in color, boggy to palpation and a considerable amount of frothy

blood-tinged fluid exuded from the cut surface. There was no evidence of consolidation. The apex of the upper lobe was torn in removal, considerably reacted by scar tissue, contained several well-circumscribed and densely fibrotic nodules which presented upon section caseous centers.

The left lung was a counterpart of the right, with the exception that the nodular involvement at the apex, while present, was less marked. This was an old process and there was no evidence of a recent flare-up.

The pericardium contained the usual amount of serous fluid, and there were no adhesions.

The heart, *in situ*, was dilated and the large vessels on the venous side were dilated and filled with blood. This dilatation involved the right auricle. The coronary vessels were partially dilated with no evidence of fibrosis.

The thymus gland showed distinctly its outline and was removed without much difficulty. Upon section the structure was somewhat dense by reason of a fibrosis, but the replacement by fat predominated. At the upper positions of the thymus and upon both sides of the vessels several large masses of darkly pigmented lymph nodes were found. There was no other involvement of lymph nodes in the neck.

The thyroid was not enlarged and its gross appearance was that of the normal pink, fleshy color and character.

Abdomen. The abdomen was flat. The omentum was thick and well nourished. This tendency to the deposition of fat was also noticed in the subcutaneous areas here at the expense of muscular development.

The usual anatomy of the abdominal cavity was preserved; the appendix was normal and the gall-bladder slightly distended, but free from adhesions. The lower border of the liver had the usual outline, being at the costal margin. The liver was a dark, slaty color with a tendency to swelling of the parenchyma. The bile ducts were patulous and free from stones.

The spleen was slightly enlarged, of a slaty gray color, and upon section the splenic pulp was dark blue with the follicles standing out distinctly.

Suprarenals. Both organs were involved in exactly the same manner and the process was sharply confined to the suprarenal bodies. There had been no extension from within outward and no evidence of surrounding involvement. *In situ* the organs occupied their usual positions, bound in a considerable amount of perirenal fat. Upon palpation they could easily be distinguished by their peculiar outline. If anything, they felt somewhat firmer than usual. There was no enlargement. Upon excision, attempting to dissect out the bodies from their surrounding fat, the usual brownish or yellowish character of the glands was found to have entirely

disappeared. Its place was taken in part by a fibrosis of the capsule and in part by an irregular trabecular type of firm, whitish tissue enclosing areas of softening more like a coagulation necrosis than an actual suppuration or caseation. The color of these softened areas corresponded to the color of the surrounding fat. If one had not been sure of the palpation of these organs and their position after excision and incision, nothing could be recognized which would fix their character. In other words the process present had involved the entire glandular structure, both cortex and medulla. The remaining substance was a mass of fat enclosing the capsule and trabeculæ of fibrous tissue enmeshing areas of necrosis. This was a most unusual finding, the picture quite definite in itself and after a minute search no evidence of other similar involvement, with the exception of the healed caseous nodules in both apices, which were like all other similar lesions, could be found.

The kidneys were small, dark blue in color, bound down in considerable fat, capsules slightly adherent, cut edges bulged distinctly, cortex granular, with paler mottled lines. The pyramids stood out as almost pallid white islands in the midst of the kidney substance. There was no involvement of the ureters or bladder.

Upon dissecting out the retroaortic vessels several masses of glandular tissue were encountered. Some of these were distinctly hemolymph node types while others presented the fleshy character of lymphoid hyperplasia.

The pancreas had the usual salmon-pink color and upon section a normal meaty character. There was no fatty replacement and no fibrosis.

Microscopical Examination. *Kidney.* The section presents the pyramidal positions with increased hyalinized periglandular connective tissue. The cortex presents dilation and stasis of red blood cells in all capillaries, especially the tubular ones. In the endothelial cells of these capillaries and in the epithelial cells of the tubular epithelium there is a deposition of refractive granules of pigment. The tubular cells are swollen and granular, with distinct nuclei. The glomerules have slightly fibrotic capsules, desquamation of epithelial cells and some reduction in the size of the tufts.

Diagnosis: Chronic degenerative nephritis with passive congestion and metabolic pigmentation.

Liver. The section presents a diffuse appearance. The lobular structure is lost by reason of diminution of perilobular tissue. This is especially true of biliary capillaries and bile ducts. Decided atrophy of these elements is present. The central lobular veins are not distended but the interlobular capillaries are the seat of a diffuse but moderate stasis. Their endothelial lining cells are filled with granular pigment. The liver cells are not sharply defined but run into one another, with some obscurity of nuclei, and positions corresponding to the central lobular veins show vacuolization of fatty metamorphosis.

Diagnosis: Chronic degenerative hepatitis with diffuse passive congestion, fatty metamorphosis, metabolic pigmentation and atrophy of biliary system.

Spleen. The section presents a diffuse appearance and does not show the prominence of follicles noted grossly. The trabeculæ are not thickened, but in places are prominent. There is a marked deposition of pigment of the same character as elsewhere, but in greater bulk. The lymphoid cells are closely packed and here and there endothelial cells have proliferated. Congestion is diffuse and stasis of red blood cells marked.

Diagnosis: Chronic lymphoid splenitis with passive congestion and metabolic pigmentation.

Thyroid. The section presents a compact picture of one of glandular activity. The epithelial cells are single layered, but show some proliferation as new glands. There are areas of lymphocytes and the capillaries are uniformly the seat of stasis of red blood cells. There is no pigment except in the endothelial cells of large vessel walls.

Diagnosis: Chronic interstitial thyroiditis with congestion.

Pancreas. The sections of pancreas present well-stained pancreatic cells, taking the usual predominance of basic color. The islands of Langhans stand out clearly. All vessels, both capillaries and large, are filled with red blood cells, the same congestion as noted in other specimens. There is a diffuse deposition of pigment throughout the section not alone confined to the epithelial cells but decidedly concentrated in the midst of the cells of the islands of Langhans.

Diagnosis: Congestion and metabolic pigmentation.

Thymus. The usual fibro-fatty tissue is present here with numerous large bloodvessels, and scattered throughout this are areas of lymphoid structure surrounding remnants of Hassall's corpuscles. The latter are small, flattened whorls of epithelial cells apparently containing congested red blood cells. In the lymph structure about these the type of cell is a small lymphocyte similar to those of the lymph node extending irregularly into the fatty connective tissue. There is no pigment present in this section.

Lymph Nodes. Numerous sections of lymph nodes taken from the peribronchial position show a large amount of pigment deposition, some of which is anthracotic, but a large amount of which is the same metabolic character as noted in the other sections. Capillaries are congested. There is a slight proliferation of lymphoid cells with irregular areas of endothelial cells, as noted in the spleen.

Retroperitoneal lymph nodes show the characteristic lymphocytic hyperplasia, congestion of the capillaries is moderate and only a small amount of pigment is present.

Sections taken from the retroaortic positions show numerous areas of lymphatic structure with markedly congested vessels. The

lymphoid proliferation is not as marked as elsewhere nor is the endothelial hyperplasia apparent.

Adrenals. There is no normal adrenal structure microscopically. There is a diffuse cellular proliferation, which cells are of several types—endothelial, plasma, endotheloid and fibroblastic. The endothelioids have grouped themselves into regular tubercle formation which in places has gone on to areas of necrotic hyaline and caseation. Here and there may be seen large giant cells. This process is not as sharply defined microscopically by the capsule of the adrenal, which in places is hyalinized, as it was apparently in the gross specimen; however, it does not penetrate to any considerable extent into the surrounding fatty connective tissue. As noted grossly the necrotic hyaline is more abundant than caseation, with a tendency to large conglomerate tubercles rather than miliary types.

Diagnosis: Caseous tuberculosis.

Guinea-pig Test. Subcutaneous emulsion of adrenal into two pigs. Both pigs died March 29, 1921. Autopsy showed identical findings. A small nodule over the site of the injection, tubercles with swelling and congestion in the spleen, liver, lungs and peribronchial lymph nodes. A small bloody exudate with some nodules on peritoneum.

Smear from Spleen: Tubercle bacilli positive.

Comment. Cases of true Addison's disease, tuberculosis of the adrenals, while they are not rare, are uncommon enough to warrant their report. In a study of this case there are several interesting features open to discussion and lines along which further work should be undertaken.

In the first place the presence of an advanced and directly confined active tuberculosis in both adrenals and the finding of a completely arrested and healed tuberculosis in the apices of the lungs is a hard one to explain. There has evidently been no fresh activity arising from the lungs. The apical infection may have preceded the adrenal infection or may have been coincident with it, or even the so-called healed lesions may have given up virulent tubercle bacilli which have secondarily lodged in the adrenals.

That this disease, at one time, must have been a bacteriemia, at least of a temporary nature, is quite evident. It would seem to the writer that the pulmonary lesions occurred at one time and were completely arrested while the adrenal lesion received its dosage through another portal of entry not apparent at the time of autopsy. The question as to whether a strain of tubercle bacilli with a predilection for the adrenal is only a supposition, and on the other hand any chemical combination which the adrenals might have had in attracting the tubercle bacilli to that particular site would, it seems to me, be a decided possibility. The complete absence of tuberculosis elsewhere in the body, in the presence of such an active lesion as found in the adrenals, offers a further field for study. That the

organisms had any predilection for the adrenal gland is more certainly ruled out by the fact that when inoculated into the guinea-pig they produced in duplicate the usual experimental tuberculosis.

The nature of the pigment, at least from its morphological character, would seem to be similar to that found in the hemozoin pigment of malaria, and indeed the distribution was very similar, being found in large quantities in the spleen and in the endothelial cells of capillaries throughout the sections.

That any of the other glands of internal secretion, as, for instance the thyroid or the retroaortic lymph nodes, were stimulated does not seem likely, although in the thyroid a distinct interstitial thyroiditis of a lymphoid nature was present.

The appearance of the capillaries in all of the sections showing a uniform stasis of red blood cells should be noted in the nature of a passive congestion with the characteristics of an active type. That the disease was due to a tubercle bacillus the case conclusively proves by animal experiment, in which the usual tuberculosis was produced and from which tubercle bacilli were cultured.

It is unfortunate that chemical studies were not carried out, either during the lifetime of the patient or upon the remnant of the adrenal gland obtained at autopsy. It would seem that the entire adrenal gland was eventually destroyed and replaced by a tuberculous process of a rather highly cellular character. That this produced a general diminution of adrenalin is quite apparent from the clinical history, but chemico-physiological studies of the gland remnant would have been interesting.

Conclusions. This report covers a case of Addison's disease presenting the characteristic clinical symptoms of progressive weakness associated with bronzing of the skin.

Pathologically the case presented a typical localized and focalized tuberculosis of both adrenals with an arrested apical pulmonary tuberculosis of a probable unassociated nature. The direct smear from the adrenal showed the presence of tubercle bacilli in large numbers. Animal inoculation with crushed material from the adrenal produced experimental tuberculosis from which tubercle bacilli were obtained in culture.

REVIEWS.

X-RAYS AND RADIUM IN THE TREATMENT OF DISEASES OF THE SKIN. By GEORGE MILLER MACKEE, M.D., Assistant Professor of Dermatology and Syphilology, College of Physicians and Surgeons, Columbia University; Fellow of the New York Academy of Medicine; Member of the New York Dermatological Society, New York Roentgen Society and Manhattan Dermatological Society; Member of American Dermatological Association, American Roentgen Society and American Medical Association; Former Editor of Journal of Cutaneous Diseases; Consulting Dermatologist and Syphilologist, St. Vincent's Hospital, etc. Illustrated with 250 engravings and 22 charts. Philadelphia and New York: Lea & Febiger, 1921.

THE first nineteen chapters, constituting about one-half of this book, are devoted to a general consideration of the physics of *x*-rays and radium, their biological effects and therapeutic action, and the method of application in the treatment of diseases of the skin. The author, unlike many others, has happily avoided the mistake of leading the reader into a bewildering maze of electrophysics that is entirely beyond the comprehension of the average physician (roentgenologists included) and leaving him stranded there, regretting all the while that he had not completed a course in electrical engineering before taking up the work of a radiologist. Instead his discussion of this phase of the work is relatively brief, but of sufficient length and detail to give a clear idea of the essential principles underlying the production of *x*-rays. The physics of radium and its emanations is treated in the same concise and clear manner. Valuable chapters in this section deal with the selection of *x*-ray apparatus, the amount and form of radium applicators, the arrangement of apparatus in the laboratory, the computation and charting of dosage, superficial and deep therapy, radiodermatitis and protection of patient and operator. The beginner will do well to study thoroughly and become familiar with the chapters dealing with burns and protection before attempting to use either the *x*-rays or radium as a therapeutic agent.

The latter half of the work is devoted to a discussion of *x*-rays and radium in the treatment of dermatological lesions, with explicit instructions as to the manner of their application. The author

very evidently realizes that these agents are productive of great harm when improperly handled and he therefore overlooks nothing in detailing his technic. He does not claim that his is the best technic that has thus far been evolved, but when one stops to consider that his knowledge is born of a vast experience accumulated by years of close study in a large clinic, we may safely accept it as standard. It surely gives us a comprehensive working knowledge such as we never before have had. The fact that conditions will doubtless arise that will warrant a modification of some of the author's methods, does not in the least detract from their value. The last, but by no means the least important, chapter deals with the medico-legal relations of roentgen and radium therapy. This chapter can be read with profit by any member of the medical profession, be he general practitioner or specialist.

The book contains one or two typographical errors, but is well written withal. The author, who is an acknowledged authority, has entirely accomplished his purpose in giving this work to the profession. He set out to produce a book in which the specialized training of the roentgenologist and dermatologist would be correlated and he has made a thorough job of it. All roentgenologists and dermatologists should be very grateful to him for having done so. J. D. Z.

TRAUMATIC SURGERY. By JOHN J. MOORHEAD, M.D., Professor of Surgery and Director, Department of Traumatic Surgery, New York Post-Graduate Medical School and Hospital. Second edition. Pp. 864; 619 illustrations. Philadelphia: W. B. Saunders Company, 1921.

THE second edition of this very useful work will be welcomed by the profession. The percentage of traumatic surgery seen by the general practitioner and the general surgeon is so constantly increasing that the importance of a wider knowledge of this subject is everywhere realized. Dr. Moorhead has revised the first edition of his work, so that this second edition includes many of the improvements gained by war experience. The subject of wounds, including bullet wounds, is dealt with in a concise and interesting chapter. The treatment of wounds according to their degree is systematically arranged, so that a novice in surgery can understand and follow it. In a similar manner the author deals with the subject of infected wounds. The Dakin-Carrel technic is given at length, together with the method for the preparation of Dakin's solution. Although the author discusses tetanus fully, he does not devote as much space to gas gangrene as the reviewer thinks necessary, especially with the ever-increasing number of cases seen in civil practice following traumatic wounds. The chapter on shock does not give adequate

attention to the value of blood transfusion in cases of shock associated with hemorrhage; however, in other respects it is admirable. The chapter on injuries of the joints includes a series of excellent roentgenograms taken from the *Murphy Clinics*, showing the blood supply in and around many of the important joints. Dislocations and fractures are dealt with in text-book style, and here again the author has included the appliances which were found of value in the treatment of military injuries. The use of the Thomas splint for fractures of the humerus and femur, together with the Blake-Keller femur splint and the Balkan frame, is carefully discussed and admirably illustrated. The only improvement one could desire for this chapter would be more attention to the caliper method of extension for fractures of the femur and both bones of the leg, since this has supplanted the "Codivilla-Steinmann nail extension method." The chapter discussing osteomyelitis falls short in its description of the treatment of chronic osteomyelitis, the author having completely omitted the excellent work of Chutro in this connection. Injuries of the head and spine have received the attention they deserve. Both subjects are thoroughly treated and the text is well illustrated. The same can be said of injuries of the chest and abdomen. It is to be regretted that the author found it necessary to include methods for nerve-lengthening and nerve-anastomosis, which, as has been said, if they do give results, are more attributable to luck than to good surgical technic. Injuries due to electricity, burns, heat-stroke, compressed air, illuminating gas, submersion and suffocation receive their proper attention. It is surprising, and yet enlightening, to see the relation of injuries to abortions, appendicitis, visceral prolapse and hernia discussed in so interesting a manner. The chapter on the traumatic neuroses should be read by everyone who has access to the book. It could not be improved upon. Standardized first-aid methods in accidents as related to industrial surgery are added in a new and final chapter. I. S. R.

PROSTHETIC DENTISTRY. By DOUGLAS GABELL, L.R., C.P., M.R.C.S., L.D.L., Dental Surgeon to the Royal Dental and Charing Cross Hospitals, Lecturer on Dental Mechanics to the University of London at the Royal Dental Hospitals. London: Oxford Medical Publication. Henry Frowde, Hodder & Stoughton, 1921.

A TEXT-BOOK of 234 pages, devoted to the chair side work for producing plate dentures. It is a book of unusual value to the student and recent graduates, as the subjects are fully and clearly treated, and would be the means of forestalling many unfortunate and avoidable failures. The concluding chapter on Complaints is a most unique, practical and useful one. P. L. L.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Acute Circumscribed Edema (Quincke).—H. QUINCKE (*Berl. Med. Klinik*, 1921, xvii, 675) analyzes 36 cases of "acute circumscribed" (angioneurotic) edema. The cases were evenly distributed among the sexes; the majority occurred between the ages of twenty-one and thirty years, the extremes being thirteen and sixty-eight years. The duration varied from a few weeks to thirty years; average five years. The duration of a single attack varied from a few hours to six days, commonly one and a half days. A single eruption lasted from ten minutes to twelve hours, the majority lasting five to six hours. The intervals between attacks varied from twenty-four hours to weeks, months or years (twenty-six years). In some cases there was some periodicity, the occurrences being daily at the same hour, or at longer intervals. A few cases showed a time relation to menstruation, either before, during, or after the period. Predisposing factors included psychic disturbances, overwork, postoperative hemorrhage, constipation, different types of food and drugs, sea-baths, warm baths, mechanical pressure, the rays of the sun, and toxins from foci of infection. Fever was present in a few cases. Thirty-nine per cent showed general nervous disturbances, and 13 per cent gave a suggestive hereditary history. A sedentary occupation seemed to be a predisposing factor in many cases. The swellings vary from 2 to 10 cm. in diameter, are raised, but not sharply marked off, either, pale, normal color, or reddened, and usually do not pit on pressure. There is a feeling of tension or burning, sometimes itching. Atypical forms and gradations of

Quincke's disease to erythema multiforme, erythromelalgia and Raynaud's disease were encountered. The most common site of occurrence of the swellings was the face (80 per cent), the eyes, lips, hands, arms, tongue coming next in frequency.

Herpes Zoster Associated with Disease of Internal Organs.—ARNSTEIN (*Wien. klin. Wchnschr.*, 1921, xxxiv, 13) describes a series of cases illustrating the occurrence of herpes zoster as the sole presenting symptom in diseases of internal organs. In an inflammatory disease of the liver, the herpes appeared along the course of the ninth thoracic nerve on the right. In a pulmonary infection in the left base, herpes appeared along the course of the fourth and fifth left thoracic nerves, later becoming generalized. In another case in which the left lower lobe was infiltrated, the lesions followed the course of the sixth thoracic nerve on the left. The course of the fifth thoracic on the right was affected in a case of involvement of the right apex, while an infection of the left apex was accompanied by a herpes at the level of the sixth left cervical nerve, and at the level of the third or fourth nerves in other cases. These areas correspond somewhat to the zones of Head, and the phenomena were explained on the basis that areas of lessened resistance resulted in the ganglia of the viscera-sensory reflex, followed by a hemorrhagic inflammation, from an infectious or toxic agent. The author suggests that all cases of herpes zoster should be examined for hidden internal lesions.

SURGERY

UNDER THE CHARGE OF

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Flocculation Reactions in Syphilis with Especial Reference to the Meinicke and Sachs-Georgi Reactions.—LEVINSON (*Am. Jour. Syphilis*, 1921, v, 414) says that a brief *resume* of the numerous studies of the Wassermann reaction discloses two schools of thought (1) that which believes that the Wassermann reaction is an antigen-antibody reaction, and has attempted to modify and simplify this reaction; (2) that school which follows the study of the chemistry of the colloids and has attempted to show a parallelism between the Wassermann reaction and certain colloidal reactions. The latter has led to the Meinicke and Sachs-Georgi reactions. The Meinicke reaction is a test based on the hypothesis that the reaction between serum and extract takes place when extract colloids disturb the isotonicity of salt solution permitting the union of seroglobulins and lipoid extracts. This reaction is greatly intensified in positive syphilitic

serums as compared with negative. The various forms of Meinicke's reactions are the water method, salt solution method, and the third method, using an antigen prepared according to the method of Wassermann with the addition of horse heart extract. The Sachs-Georgi reaction is a physicochemical reaction between seroglobulins and lipoid extracts. Phases 1 and 11 of the Meinicke reaction showed 89.2 per cent agreement with the Wassermann reaction; this reaction is in all respects characteristic for syphilis and it is more simple than the so-called third modification or Sachs-Georgi reaction. The third modification of the Meinicke reaction is more simple and is therefore recommended. The agreement with the Wassermann reaction is 88.8 per cent. In many cases it is positive earlier and often remains longer than the Wassermann reaction. The Sachs-Georgi reaction has met with the approval of many investigators. The non-specific reactions are less frequent with this test. None of these reactions can at present supplant the Wassermann reaction, but may be used in conjunction with it.

Viability of Spirocheta Pallida in Excised Tissue and Autopsy Material.—LACY and HAYTHORN (*Am. Jour. Syphilis*, 1921, v, 401) say that from their experiments it is evident that spirochetes kept in serum or moist tissue, either human or animal, may retain slight motility as long as three months or more. Reliable dark-field examinations can be made on tissues or fluids collected several hours previously, provided they are kept moist and cool. The authors' results, which are in accord with those of Neisser, would indicate that complete drying is probably fatal to the Spirocheta pallida, since each of the rabbits inoculated with dried spirochetes on scalpels failed to develop syphilitic lesions. Spirocheta pallida may and in the author's case did remain virulent in autopsy material for twenty-six hours or longer.

Complement-Fixation Tests with Two Antigens.—LARKIN (*Am. Jour. Syphilis*, 1921, v, 476) says that two antigens whose reliability has been established form a valuable check upon another for routine public health laboratory work. Cholesterinized antigen gave a high percentage of positive and doubtful reactions. This bears out the usual observation that cholesterinized antigens are more sensitive than crude alcoholic antigens. Sera are occasionally found which are undoubtedly positive but which, due to some peculiarity of the serum do not react with one of the antigens used. The cholesterinized antigen, used alone, must be considered a rather unreliable antigen likely to give false positives.

Studies in the Standardization of the Wassermann Reaction.—KOLMER (*Am. Jour. Syphilis*, 1921, v, 439) says that the antibody content of serum from mixed venous and arterial blood collected by pricking a finger and of venous blood collected by venipuncture, is identical. Blood sera collected from fingers or by cupping are more likely to become anti-complementary than sera collected by aseptic technic and venipuncture, due to greater chances for bacterial contamination. Syphilitic sera collected at once by defibrinating and centrifuging blood contain as much complement-fixing antibody as

sera allowed to separate from one to forty-eight hours. When preserved human sera yield stronger complement-fixation reaction than the same sera while fresh, the difference is due to the presence of anti-complementary substances antilysins or the deteriorations of natural hemolysins. The anti-complementary activity of a serum is greatly modified by whether it is used unheated or heated and by the presence or absence of natural hemolysins. The presence of anti-complementary substances (antilysins) influences the degree of positiveness of a reaction and explains in part the differences observed with portions of the same blood in different laboratories; technic should, however, discover the presence of these antilysins and render all laboratory reports uniform, insofar as positive or negative reactions are concerned. The serum control tube should not carry more serum or spinal fluid than the main tube or tubes if an anti-sheep or anti-ox hemolytic system is being employed in order to avoid the influence of natural hemolysis.

Salt Solution in Increased Intracranial Tension.—FOLEY (*Surg. Gyn. Obstet.*, 1921, xxxiii, 127) says that intravenous injection of hypertonic salt solution or the ingestion of salt produces a fall of cerebrospinal fluid pressure and a diminution of brain bulk. In conditions of pathologically increased tension, the response is conditioned by the details of the pathological alterations. The determining factors appear to be the size of the lesion which increases brain bulk and the amount of fluid available for absorption. The induced fall of pressure is inversely proportional to the former and directly proportional to the latter. A distinction is made between increased intracranial fluid tension *per se* and increased intracranial tension which is due to enlargement of brain bulk. From observation of cases of obstructed and dilated ventricles an intraventricular absorption of fluid following salt ingestion seems to occur. The procedure has a definite field of clinical usefulness in cases exhibiting high grades of intracranial pressure. The most striking results are to be obtained in those cases in which cerebrospinal fluid obstruction exists.

Jejunal Ulcer.—JUDD (*Surg. Gyn. Obstet.*, 1921, xxxiii, 120) says that gastro-enterostomy for ulcer of stomach or duodenum offers the patient a good prospect of complete and permanent relief of all symptoms. Unsatisfactory results are most often due to a gastro-jejunostomy in cases in which no ulcer exists—procedure must be upon a pathological basis. The relative appearance of the syndrome called "vicious circle" is due to recognition of the importance of avoiding operation when no ulcer exists. Jejunal ulcer is one of the most serious and perhaps one of the most common after-complications of gastro-enterostomy. It occurs either in the line of anastomosis as a so-called gastrojejunal ulcer or in the jejunum as a true jejunal ulcer. The lesion is usually single. Its frequency is difficult to estimate, Patterson reporting that they occurred in from 1 per cent to 2 per cent of cases. A satisfactory explanation of the cause of jejunal ulcer can best be found in the etiology of the original ulcer. Only one case of primary jejunal ulcer is mentioned in the literature. The author notes that jejunal ulcer following operation almost always occurs only following gastro-

enterostomy for ulcer. There have been no cases observed in the Mayo Clinic following plastic procedure around the pylorus. The principal cause of the secondary ulceration is the action of the acid gastric secretion on the mucous membrane of the jejunum. In all Patterson's cases and in more than 60 per cent of the cases in the clinic the acids were high even after gastro-enterostomy. Permanent suture material has also been a factor in the production of many ulcers particularly those close to the gastro-jejunostomy opening. Infection must play some part in the etiology of these lesions, for the cut surfaces of the stomach and of the jejunum are exposed to the infection from the original ulcer during operation and during the healing process, which lasts about fourteen days. The onset of symptoms varies from almost immediately after the gastro-enterostomy to eight or ten years. Usually all symptoms are completely relieved following gastro-enterostomy for six months to a year. The results of operations in these cases of secondary ulcer have been reasonably satisfactory, especially since the importance of dispensing with the gastro-enterostomy has been realized. Whenever a secondary ulcer has formed after gastro-enterostomy it is surprising how many will continue to form if the anastomosis is maintained in those patients who seem to have some definite irregularity or specific infection.

Studies in Reduction of Bone Density.—PHEMISTER (*Am. Jour. Roentgenology*, 1921, viii, 355) says that reduction in density may be local, regional or general—according to the cause. The author's object is to show the histologic processes by which bone is destroyed. In bone infections there are four processes by which reduction in density may be produced—first, there is destruction of dead bone at the seat of greatest inflammatory activity; second, there is local destruction of living bone or caries; third, there is rarefying osteitis in the neighboring living bone for variable distances about the area of complete bone destruction; and fourth, there is regional atrophy of disease. In osteomyelitis necrotic bone results from the effect of the toxins in the most severely inflamed region. The unossified elements of the dead bone are rapidly killed by toxins and removed by the action of the serum and leukocytes. The calcareous deposits are only removed as a reparative process by the absorptive action of the granulations. From six to fifteen days elapse before signs of reduction in density can be shown by the *x*-ray. Tuberculosis usually produces localized osteitis. The metaphyseal region of the end of the bone is more frequently involved primarily, especially during the first decade. After the tenth year primary foci in the epiphyses are seen with increasing frequency. Ingrowth of tubercular granulation tissue beneath the articular cartilage is a common occurrence leading to destruction of the articular cortex of bone and to disappearance of the sharp line which it normally casts in *x*-rays. Bone syphilis produced gummatous caries in irregularly distributed and various-sized areas. Shadows from new bone formation are frequently interspersed. In bone tumors reduction of density results almost entirely from breaking down of living bone by cellular activity. In metastatic carcinoma of bones the relative amounts of bone destruction and new bone formation bear some relation to the seat of the primary tumor—and its degree of malignancy

and rate of growth. Metastatic carcinoma of the breast tends to produce bone destruction with little associated new bone formation, while carcinoma of the prostate produces little bone destruction and much new bone formation. Reduction in density in sarcoma usually occurs *en masse* and while the outline of the area destruction may be irregular, extensive pocket formation is uncommon. New bone formation in the ossifying types of sarcoma may be sufficiently extensive to offset the reduction in density resulting from bone destruction but its distribution and arrangement are usually such that the shadows cast are of diagnostic significance. Central giant-celled tumors affecting the ends of the living bones form a special group and it is questioned whether they should be classified with sarcomas. They reduce bone density by eccentric growth and are entirely devoid of any tendency to undergo ossification. The reduction of density in bone cysts is quite similar to that in giant-celled tumors in that the process begins in the interior of the bone and produces eccentric erosion without subsequent ossification of the tissue which caused the erosion. Small perforations of the cortex are more common. The site affected is farther from the bone end.

PEDIATRICS

UNDER THE CHARGE OF

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A Contribution to the Topographic Anatomy of the Thymus Gland with Particular Reference to its Changes at Birth and in the Period of the Newborn.—NOVACK (*Am. Jour. Dis. Children*, August, 1921) studied 65 fetuses and full-term children. He found that the lobation of the thymus is determined early in fetal life, and the establishment of respiration has no effect on it. The thymus in the late fetus and in the newborn is predominatingly of the cervicothoracic type, with the position intermediate between the cervical location in the embryo and the thoracic location of the older infant child and adolescent. In the late fetus and in stillborn children there is a typical form and quite constant relations. Its lateral surfaces are convex and bulge against the medial surfaces of the lungs. The lungs very rarely extend at all on its anterior surface and the thymus very rarely extends at all on the anterior surface of the right ventricle of the heart. In liveborn infants it has a typical form and relation which are similar to those found in young children. It is elongated and molded so that the anteroposterior and lateral surface bear the impressions of all the organs with which it is in contact. The lateral surfaces usually show marked convexities, which are occupied by the lungs, which pass over the anterior surface of the organ. Unlike the fetal thymus it usually extends more inferiorly, passing over the right ventricle. The change from the broad or fetal type to the elongated and molded type found in the liveborn and in

young infants bears a direct relation to the establishment of respiration and is dependent on the expansion of the lungs. The organ is compressed from side to side by the medial surfaces of the expanding lung. It is compressed anteroposteriorly by the anterior borders of the lungs, which become much thickened in the establishment of respiration as they gradually overlap the thymus. In some cases the thymic substance may project posteriorly at birth to such an extent that some of the structures situated there are compressed by it. This may be due either to an unusually large thymus or to a very narrow superior thoracic aperture which will not allow the thymus to protrude into the cervical region as it is compressed by the expanding lungs. A distinction should be made between the broad fetal type and the infantile or narrow elongated type.

Calcium and Phosphorus in the Serum in Relation to Rickets.—Howland and Kramer (*Am. Jour. Dis. Children*, August, 1921) found that in non-rachitic children the concentration of calcium is from 10 to 11 mg. per 100 cc of serum. The concentration of inorganic phosphorus is about 5 mg. per 100 cc of serum. The constancy of the concentration of calcium, phosphorus and bicarbonate in the serum of normal children undoubtedly determines the constancy of the inorganic composition of normal bone. During the period of active rickets the calcium concentration may be normal or slightly reduced. The reduction does not seem to depend directly on rickets. There are reasons for believing that in many instances the reduction is related to a latent form of tetany. The inorganic phosphorus of the serum is regularly reduced in active rickets, sometimes to an extreme degree. During the process of healing, whether occurring spontaneously or as the result of the administration of cod-liver oil, the phosphorus content of the serum gradually rises to a normal figure and often somewhat above this. Relapses are accompanied by a fall in the phosphorus concentration of the serum. All the children under two and a half years of age in whom there was an inorganic phosphorus content of the serum of 3 mg. or less had been suffering from rickets.

The Casein of Cows' Milk and Human Milk in their Relation to Infant Feeding (the Action of Rennin on Casein).—Bosworth (*Am. Jour. Dis. Children*, August, 1921) found that the casein from cows' milk and human milk are acids, having the same chemical composition and the same chemical characteristics, the two caseins forming the same series of salts with bases. In cows' milk the casein is present as a calcium caseinate, while in human milk the casein probably is present as a potassium caseinate. When rennin is added to solutions of casein or to milk the casein is split into two equal molecules of paracasein. The addition of rennin to solutions of casein or to milk may or may not result in coagulation, depending on the nature of the salts in the solution or milk. Coagulation is promoted by soluble calcium salts and is retarded or inhibited by the addition of soluble salts of sodium, potassium or ammonium. The development of acidity in cows' milk favors coagulation after the addition of rennin; the greater the acidity the tougher the curds. Milk in entering the infant's stomach is acted upon by the enzymes present. The enzyme rennin, acting upon casein,

changes it to paracasein. Breast milk contains small amounts of casein and small amounts of soluble calcium with relatively large amounts of sodium and potassium. The action of rennin on breast milk results in no curdling or the production of a very small amount of very finely divided curds. Breast milk enters the mouth, stomach and intestines in a liquid state. It does not form large curds in the stomach and cannot block the pylorus. Cows' milk or any of its modifications contain large amounts of casein and soluble calcium with relatively small amounts of sodium and potassium. The action of rennin on these milks or their modifications, owing to the high casein and soluble calcium contents, results in the production of large flocculent curds, which at body temperature may coalesce and form large masses. These masses are a mixture of paracasein, fat and milk salts. Cows' milk or any of its modifications enters the mouth and stomach as a liquid, but in the stomach a part of the milk may be separated into curds by the action of the rennin. These curds may become very large and may block the pylorus. They may remain in the stomach for days and may be added to by subsequent feedings. Fresh cows' milk does not curdle on addition of rennin. Curd formation depends on acidity.

Lesions of the Corpus Striatum in Childhood, with a Report of Clinical Cases (Illustrating Various Syndromes).—CROTHERS (*Am. Jour. Dis. Children*, August, 1921) says that a number of syndromes characterized by disturbances of associated movements, variation in muscle tone and speech defects are definitely associated with sharply defined localized lesions of the corpus striatum. They are easily distinguished in typical cases from spastic pyramidal tract syndromes and from ordinary chorea. In atypical cases confusion arises and careful sorting out of signs is necessary. Critical reëxamination of children showing involuntary movements over a period of months or years reveals unsuspected cases. The cases of this series demonstrate the dangers of relying on casual impressions in judging mental states when speech defects and motor disorders complicate the picture. From every point of view the study of cases of the type described here is well worth while. The present classification is purely tentative and is too rigid. The author's experience indicates that these disorders are not rarities, but that general attention to them has not been stimulated. The corpus striatum may not be the only area involved. Many other lesions may complicate and obscure the picture.

Some Observations on the So-called Inanition Fever of the Newborn.—GRULEE and BONAR (*Arch. Ped.*, July, 1921) reported at the meeting of the American Pediatric Society that they had studied 183 newborn infants with regard to the transitory fever which frequently occurs during the first few days of life, and which has not been accounted for satisfactorily. It is apparently a febrile condition simple in nature. Observations were made on the weight for the first five days; the percentage of greatest loss; the highest daily temperature for five days; the quantity of breast milk for this time period; the quantity of water for the same length of time; the total foods taken for these days; the estimated loss by vomiting; the total number of stools; icterus if present and upon what day it appeared. The cases were divided into groups

according to weight. For normal cases the average weight loss was 6.2 per cent; for 46 cases with a temperature between 99.2° and 100° the weight loss was 6.2 per cent; for 16 cases with a temperature between 100.2° and 102°, the average weight loss was 11.2 per cent. While at first glance this appeared to be significant, if the individual cases were carefully examined it would be found that among the cases with normal temperature the loss of weight was as great as 17.3 per cent, which was higher than any case with fever. There could not be shown any regular relationship between the quantity of fluids ingested and the occurrence of fever. Some cases seemed to show a relationship between the fever and the food ingested, but others seemed to give an opposite result. The conclusion was made that the temperature rise was not regularly to be explained on the basis of dehydration. It has been suggested that he temperature elevation may be due to the absorption of some protein product, either bacterial or other.

Malnutrition in Children of the Well-to-do.—KERLEY, LORENZE and DUBOSE (*Arch. Ped.*, July, 1921) presented this paper at the meeting of the American Pediatric Society. They described a type of cases of malnutrition where the child remained persistently an inferior individual from a physical standpoint. In the majority of these cases two features stood out prominently. These were deficient food intake or imperfect digestion, though the caloric intake was not necessarily below the normal requirements. It was found that these cases fell into groups. First there were those cases in which there was a maladjustment of the different food elements. Usually butter cream and 4 per cent milk fat had been crowded. From the caproic standpoint the children had been fed above their requirements on a non-growing diet. The essential foods, meats, cereals, vegetables and fruits were taken indifferently. In the management of these children the fact must be recognized that there must be a healthy desire for food, and this can be created by the withdrawal of fats and sugars in large measure. Three meals should be given daily at five-hour intervals, and nothing but water should be allowed between meals. A low fat and sugar diet should be given. In the second group hyperacidity of the stomach juices causes a defective food intake and malnutrition largely through the production of a poor appetite. The chief symptom of hyperacidity is a lack of desire for food. In cases of long standing this is accompanied by nausea and vomiting. Pain and discomfort are greatest before the meals. Gastric analyses were made in 51 cases between the ages of two and eight years. A total acidity ranging from 38 to 138 was found. Normal acidity is usually considered as ranging from 30 to 40. In this group etiological factors include candy and ice-cream, irregularity in meal hours and faulty feeding. This type of patient usually responds to dietetic treatment. Three meals suitable for the age are to be given and nothing is allowed between meals except water. Extremes of heat and cold should be avoided. Condiments, candy, pastry and raw fruits are excluded. It is important that a daily evacuation of the bowels be ensured. The third group of cases comprise those in which defective intestinal mechanics delay the emptying of the stomach. Defective food intake and poor appetite are usually found in those in whom there is a stomach residue after four and a half hours. In order that a child have a normal

desire for food there must be an interdigestive period of at least one hour. Retention is sometimes due to pylorospasm caused by an anomaly or lesion lower down in the intestinal tract. Some of these include ptosis, angulation, dilatation and sacculation. The fourth group, although comparatively small, include the hardest type to effect relief. These were the underweight, overactive, anemic, physically retarded, precocious children.

Acute Rheumatic Fever and Its Variants in Childhood and Adolescence.—RIESMAN (*Jour. Am. Med. Assn.*, May 21, 1921) points out that in childhood this disease presents certain important peculiarities. Although it occurs in children of all ages, even having occurred intra-uterine, it is most frequent between the ages of five and fifteen years, and is especially common about the age of puberty. Girls seem to be affected a little more frequently than boys, while in the adults the males are more frequently affected. The joint involvement is often slight and may be overlooked. He reminds us that growing pains, so called, are frequently rheumatic signals. The involvement of the heart is very common in children. Its occurrence and severity bear no relationship to the severity of the joint involvement, as slight joint involvement may be followed by severe damage to the heart. Follicular tonsillitis frequently precedes the attack and is commonly found in the previous history of the patient. Chorea often follows attacks. In children there is more frequently skin manifestations than in adults. Cerebral rheumatism characterized by delirium and hyperpyrexia is rarely seen in children, but it is a complication of the disease in the adult.

OBSTETRICS

UNDER THE CHARGE OF

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Treatment of Sterility by the Use of the Intra-uterine Stem Pessary.—RAWLS (*Am. Jour. Obst.*, February, 1921, p. 499) publishes the result obtained by the study of 205 cases with final results in 117 cases. In 47 cases, or 22.9 per cent, sterility was the condition for which relief was sought; in 23, or 11.2 per cent, dysmenorrhea and sterility were the reason for the treatment. In some of the cases before the pessary was introduced dilatation and curetting were done. When the scraping were examined microscopically they were normal in 68.8 per cent. The hard-rubber stem pessary was used in 54.8 per cent of the cases, the glass stem in 43 per cent, the straight in 40, the curved in 40 and the Wylie drain in 4 or 2.2 per cent. In 124 cases the pessary was worn in 16 less than a month; in 36 from one to two months; in 24 from two to three months; in 15 from three to four months; in 3 four to five; in 1 five months and in 29, or 23.4 per cent, the pessaries were cut out

partially or entirely. When hard-rubber pessaries were used sutures of silkworm gut were employed to keep them in place; when glass pessaries were selected suspension sutures were secured by shot or washers or bone buttons. While many of the symptoms and conditions present are of interest the obstetrician has to do only with the question of the use of this pessary as an aid in remedying sterility. It was found that the method of treatment has a limited field of usefulness and in about half of the patients presenting themselves with pelvic conditions this pessary could be used. As an operative measure it is applicable to 2.3 per cent of patients treated and 1.3 per cent of operations performed in hospital. The treatment is not without its complications and disadvantages, for while a temporary rise of temperature is not unusual there is a transient morbidity of 17.6 to 21.8 per cent and a permanent morbidity of from 5.8 to 9.8 per cent. For sterility it is stated that relief followed its use in 23.4 per cent. Comparing it with other forms of operative interference it is said to give as good results as other operations, with less primary invalidism and no more liability to permanent bad results. This treatment should never be used except in carefully selected and studied cases, when its results should be correspondingly good.

Indirect Expulsion of the Placenta.—Baer (*Jour. Am. Med. Assn.*, February 26, 1921) expresses the placenta by taking the abdominal wall in the two hands, drawing it together and compressing the uterus in longitudinal direction. This is done just above the uterus in such a way as to force the uterus down toward the pelvic brim; the patient is urged to bear down during this time. By this manipulation the recti muscles are pulled together and held firmly. Four hundred cases were so treated by nineteen operators. In the majority of cases this method was successful within thirty minutes after delivery of the child; in eleven cases forty-five minutes elapsed and in one case three trials were made and the placenta expressed in sixty minutes after the birth of the child. The method is stated to be 90 per cent efficient in the hands of different operators.

GYNECOLOGY

UNDER THE CHARGE OF

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Drainage in Pelvic Surgery.—The question of when to drain in the performance of pelvic operations is a never-ending question and from the extreme of universal drainage of some years ago, the pendulum has

almost swung to the point where drainage had to be defended by the surgeon using it. The question can only be answered by long and varied experience under all sorts of conditions and there is probably no gynecologist in this country whose opinion along this line should bear more weight than Kelly's (*New York Med. Jour.*, 1921, cxiv, 390). He feels sure that from time to time the judicious use of a drain over a short period of time, from thirty-six hours to several days, does one of three things: It is an unspeakable comfort to the surgeon to be sure that there is no collection of fluids about the field of operation. It relieves the patient of a vast amount of discomfort in her early convalescence, converting a stormy, febrile recovery into a smooth, peaceful one. It carries off the serum and blood, and, it may be, lingering infections which occasionally give rise to a general peritonitis. Kelly would drain in every case where infectious material has been widespread and there remain some lingering suspicions areas. He includes here cases in which there has been soiling by bowel contents. He would drain in all ragged cases such as those in which pelvic adhesions had been so extensive and firm about the floor and walls that the occurrence of considerable serosanguineous weeping is a moral certainty. Without exception, he drains after removing a cancerous uterus. He uses a small, special drain in most cases of myomectomy, where sometimes weeping and bleeding occur unaccountably. When in serious doubt, Kelly says "drain!" Some surgeons would undoubtedly reverse this dogma. If the trouble in the pelvis is very severe, then a good, big drain of washed iodoform gauze in protective rubber tissue ought to be laid through the vaginal vault, to cover the pelvic floor loosely. It should never be packed in tightly and never, under any circumstances, should the drain be allowed to extend up or down between loops of bowel. A form of drain which he has found most useful in his work, and which he calls a provisional or tell-tale drain is a small drain about the size of a cigarette or a little larger. It is peripheral in two senses, it is laid through the abdominal wall at or near the lower angle of the median incision, above the symphysis, reaching well within, but no attempt is made to come into contact with the field of the operation which lies, it may be, well below the pelvis. He uses such a drain in myomectomy as well as where serious oozing is to be expected, but never where there is reason to expect immediate infection. Its sole function is to let out all the excess of serum and blood welling up from the pelvis and seeking this direction of least resistance. It is temporary in character, being removed in from twenty-four to thirty-six hours, as soon as the outward flow abates, as shown by the dressings remaining dry.

Embolism after Hysterectomy for Myoma.—A patient has had a hysterectomy for a uterine myoma and has had a satisfactory recovery and is about to be allowed out of bed, the family having been assured that complete recovery is merely a matter of time, when suddenly, the patient collapses and death ensues in less time than it takes to describe. Such is the sad picture of pulmonary embolism as it occurs in a small percentage of cases following pelvic operations and we stand helplessly by when the condition occurs, realizing that our efforts are futile. Any investigation which would reduce the incidence of such a dreaded complication would undoubtedly receive recognition from the

profession and therefore we desire the reader to become acquainted with the work of Farrar (*Am. Jour. Obst. and Gynec.*, 1921, ii, 286) based on observations in the Woman's Hospital in New York. She finds that pulmonary embolism or thrombosis is the most frequent cause of postoperative pulmonary complications following hysterectomy for myoma uteri and the source of the embolism is a thrombosis of the pelvic veins or the veins of the lower extremities, or a thrombosis of the right heart. The development of a thrombosis or embolism may be during an operation or immediately following it. The most frequent time seems to be during the first forty-eight hours. The symptoms in the order of their most frequent occurrence are pain, friction rub, cough, bloody sputum and rales, dulness and alteration of breath sounds. These signs are premonitory of a thrombosis but the evidences of thrombosis in the veins of the lower extremity or pelvic veins do not appear until later. The physical findings at the onset are similar to lobar pneumonia or pleurisy, but the clinical picture soon separates the cases. In differential diagnosis the roentgen ray may be of value. The causes of thrombosis are: (1) An enfeebled circulation due to: (*a*) dilated venous trunks, especially of the pelvis and lower extremities; (*b*) venous stasis; (*c*) lowered blood volume due to hemorrhage or shock; (*d*) myocardial insufficiency. (2) Infection. The treatment of this condition should be prophylactic and directed to improving the circulation of the blood by strengthening the heart muscles and walls of the blood-vessels and increasing the hemoglobin of the blood. The importance of rest in bed as a preliminary to operation to relieve the pressure of large myomata on the veins of the pelvis and lower extremities, the use of blood transfusion *before* operation in cases of marked anemia and the maintenance of the blood volume during operation by gum glucose given intravenously, should be emphasized. In substantiating this theory, Farrar reports that during a two-year period all ward patients having large fibroids were kept in bed from five to seven days prior to operation and no embolism or thrombosis occurred in any case. In the private patients, who were not kept in bed prior to operation, a fatal embolism occurred once and venous thrombosis six times during the same period with exactly the same operative technic.

Management of Renal Tuberculosis.—Looked at broadly the development of our knowledge of renal tuberculosis within the last ten years has been satisfactory, according to CABOT (*Minnesota Med.*, 1921, iv, 354). The relative frequency of the disease, its accurate diagnosis and its satisfactory operative treatment have been developed progressively and soundly, and the improvement is nowhere better shown than in the operative mortality. Prior to 1900 the mortality for nephrectomy for tuberculosis was at least 25 per cent, while at the present time the mortality in the great clinics is between 2 and 3 per cent. Considering the technical difficulties of the operation of nephrectomy, the proximity of important structures, including the great blood-vessels and the rather poor condition of these patients, this is a highly satisfactory showing, and we might be satisfied if we did not turn our attention to the end-results. The study of the results in several large series of cases taken from various clinics where results are known after a lapse of years shows that we cannot yet rest from our labor. Roughly

speaking it shows that of 97 to 98 per cent of the cases who leave the hospital after nephrectomy for tuberculosis about 25 per cent die of urinary tuberculosis, and of this number one-half die within the first two years and the balance within five years. In such cases the author believes that they either had tuberculosis of the remaining kidney, though unsuspected, or they must have developed it very promptly after operation. There is no method now at our disposal which will enable us to diagnose "closed" tuberculosis, not the form in which closure of the ureter has resulted, but those tuberculous lesions of the kidney which are contained entirely within the renal parenchyma and communicate at no point with the renal pelvis. These cases undoubtedly exist and show a urine indistinguishable from the normal. As a result of his study of the problem the author believes that in a certain number of the cases we must expect tuberculosis of the remaining kidney as an unavoidable consequence of the operation, and he states there is nothing which we can do to avoid its occurrence, and it must therefore be charged off to depreciation. There is another possibility of infection occurring after operation, namely, infection of the remaining kidney as a consequence of the measures taken to arrive at an accurate diagnosis. Diagnosis of sufficient accuracy to warrant operation depends inevitably upon cystoscopy and ureteral catheterization. The majority of these patients have tuberculosis of the bladder secondary to their renal disease. In many of them the technical difficulty of the examination is great and trauma nearly or quite unavoidable, and were we dealing with any other form of infection of a unilateral type we should be gravely conscious of the danger of infecting the remaining sound kidney. This has been largely overlooked, and though it may be regarded as inevitable to accurate diagnosis, we must overhaul our methods and be sure that they expose the patients to the slightest possible danger of infection.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Experimental Rickets in Rats. I. A Diet Producing Rickets in White Rats and its Prevention by the Addition of an Inorganic Salt.—SHERMAN and PAPPENHEIMER (*Jour. Exper. Med.*, 1921, xxxiv, 189) indicate advantages of using rats for the experimental study of rickets, calling attention to the close resemblance of the lesions to those of human rickets, the ease with which controls of the same litters can be obtained, the rapid development of the lesions, the elimination of

variations in susceptibility, the possibility of working with large numbers, the economy of space and expense and finally the easy manner in which histological examination of bones can be carried out. With no failures fifteen rats were rendered rachitic by a diet consisting of patent flour (95 per cent), calcium lactate (3 per cent), sodium chloride (2 per cent) and in some ferric citrate (0.1 per cent). The substitution of 0.4 per cent secondary potassium phosphate in the diet completely inhibited the development of rickets. Quantitative determination of calcium in the bodies of parallel rats showed a marked increase of calcium content in the rats receiving the added phosphate over those which developed rickets. "While it was shown by the roentgen rays, by histological examination and by quantitative chemical analysis that added potassium phosphate increased the assimilation and normal depositions of calcium, it may be the quantitative relationship between the inorganic ions rather than actual deficiency of any one of them which was here the determining factor in the cause or prevention of rickets." The authors state that their experiments and conclusions do not exclude the possibility of other causes of rickets than those discussed by them.

Note on the Preservation of Stock Strains of Treponema Pallidum and on the Demonstration of Infection in Rabbits.—BROWN and PEARCE (*Jour. Exper. Med.*, 1921, xxxiv, 185) have been able to dispense with serial transfers of stock strains of Treponema pallidum by keeping a sufficient number of infected animals to guard against loss of the strain by their death. When it is desired to recover the organism a popliteal lymph node may be excised, aseptically, minced, ground in a mortar and an emulsion prepared by the addition of 1.5 cc sterile normal salt solution. One half cc of this emulsion is then injected into a testicle of one or more rabbits. The inoculation should be made six to eight weeks before the organism is needed. The same method is applicable for the demonstration of infection in experimental animals. The authors caution that atrophy of the testis may occur instead of the usual granulomatous enlargement and, in exceptional instances, infection may be recognized by the development of an adenopathy when no lesions can be detected at the site of inoculation. The method is based on the experimental evidence that there was a constant invasion and localization of the organism in the superficial lymph nodes, that the infection persisted indefinitely and that the organism could be recovered at any time from such nodes as the popliteals.

Bacteriologic Studies of the Upper Respiratory Passages.—In a series of four articles PILOT and PEARLMAN (*Jour. Infect. Dis.*, 1921, xxix, pp. 47, 51, 55 and 62) report bacteriological investigations to determine the incidence of hemolytic streptococci in the adenoids and of pneumococci, non-hemolytic streptococci, influenza bacilli (Pfeiffer), diphtheria bacilli and diphtheriods in the tonsils and adenoids. From cultures of 25 nasopharyngeal swabs and the surfaces of 78 extirpated adenoids from children hemolytic streptococci were recovered in 55 per cent, while from the crypt-like depressions of the adenoids of the same persons they were found more abundantly in 61 per cent. The excised tonsils of the same persons revealed hemolytic streptococci in

large numbers in 95 per cent. In a series of 103 adenoids pneumococcus occurred in 65 per cent,—2 per cent of which were type II, 13 per cent type III and 85 per cent type IV. In the nasopharyngeal swabs of 21 persons the pneumococcus was recovered in 71.4 per cent and from the tonsils of the same persons in 66 per cent and the adenoids in 71 per cent. They occurred more numerously in the crypts than in the swabs. Streptococcus viridans was found in 89 per cent of adenoids and 81 per cent of tonsils, while Streptococcus mucosus was encountered in 3 per cent of adenoids and indifferent streptococci in 12 per cent. Mather's coccus was noted in 17 per cent of adenoids. Gram-negative, pleomorphic and hemoglobinophilic bacilli, presumably Bacillus influenzæ, were isolated in 40 per cent of extirpated adenoids and in 53.9 per cent of excised tonsils from 115 persons. In the nasopharynx they were present in 40 per cent of 25 persons. B. diphtheriæ were found 12 times in the excised adenoids and extirpated faucial tonsils of 100 children, being encountered in both the adenoids and tonsils of the same individuals. Two of the 12 strains were virulent. Diphtheroids occurred in 30 per cent of the adenoids and in 17 per cent of the tonsils. In an additional investigation, MEYER, PILOT and PEARLMAN (*Jour. Infect. Dis.*, 1921, xxix, 59) found that removal of the tonsils and adenoids in children decidedly reduced the number of hemolytic streptococci and influenza bacilli, and to a less extent the pneumococci in the oropharynx and nasopharynx, but did not cause their disappearance.

Relation between the Virulence of Streptococci and Hemolysin.—STEVENS, BRADY and WEST (*Jour. Exp. Med.*, 1921, xxxiii, 223)determined the relation between the hemolysin production and the pathogenicity of five strains of Streptococcus pyogenes (Holman). Avirulent organisms were obtained by frequent transplants on blood agar for several months. The same strains were rendered virulent by repeated passages through mice, after which the virulent and avirulent forms were transplanted to horse serum broth, and fourteen to eighteen-hour cultures were seeded into trial flasks of the same media. After centrifuging, the supernatant fluid was titrated against mouse cells to determine the hemolytic titer and this was done at frequent intervals until after the maximum hemolysin production had occurred. In this way, determinations were made with actively growing organisms which were accustomed to the media in which the tests were made. The results showed that both the virulent and avirulent forms of each strain produced, at some time during their growth, approximately the same maximum hemolytic titer. There was a tendency for the original culture to grow more rapidly than the more pathogenic forms and to reach the height of hemolysin production at an earlier stage during the growth of the culture.

Acute Respiratory Infection in Man Following Inoculation with Virulent Bacillus Influenzæ.—During the past few years a large number of persons have submitted themselves to inoculation experiments where filtered or unfiltered nasopharyngeal secretions from individuals with influenza, as well as pure or mixed cultures of the ordinary bacteria, have been instilled into the upper respiratory passages. Following the observations of Blake and Cecil on monkeys, CECIL and STEFFEN

(*Jour. Inf. Dis.*, 1921, xxviii, 201) inoculated healthy human volunteers with strains of B. influenzæ, extracts of B. influenzæ, Streptococcus hemolyticus and pneumococcus. Six persons received suspensions of B. influenzæ, freshly isolated from chocolate blood agar cultures or from the peritoneal cavity of monkeys or from chocolate blood broth cultures. One volunteer was a carrier of influenzal bacilli, while three of the six had had influenza in 1918–19. All materials were administered into the anterior nares in a small quantity of fluid (0.5 to 1 c.c.). It was found that the virulent influenza bacilli excited in the volunteers "an acute respiratory disease similar in many respects to influenza, but falling short of the typical clinical picture." The authors suggested that their success could be attributed to the fact that freshly isolated, virulent strains were used and believed that fluid cultures and washings from animal exudate produced better results. Influenza bacilli, biologically identical with those inoculated could be recovered from the discharges as long as symptoms persisted and often for some time thereafter. Two individuals received filtrates of B. influenzæ cultures, both of whom showed neither local nor constitutional reaction. One of the two volunteers who were given virulent hemolytic streptococci from human sources developed an acute tonsillitis. Negative results were obtained in the two persons who received a virulent pneumococcus type IV.

Experimental Studies of the Nasopharyngeal Secretions from Influenza Patients.—Much has appeared concerning the cause of epidemic influenza in the recent literature. Positive and negative results have been obtained by various investigators employing Pfeiffer's bacillus and other organisms as well as unfiltered and filtered nasopharyngeal washings in both man and animals. OLITSKY and GATES (*I, Jour. Exp. Med.*, 1921, xxxiii, 125) inoculated rabbits with unfiltered nasopharyngeal washings, filtered washings, lung tissue suspensions (filtered and unfiltered) from previously inoculated rabbits, similar lung tissue preserved in sterile 50 per cent glycerol, bacteria and culture materials and control materials. Three c.c. of these materials were introduced directly into the lungs under light ether anesthesia, through an intratracheal catheter, by a modified Lamar and Meltzer method or by tracheotomy. The studies were performed during the first epidemic wave in 1918 and 1919, the second of the autumn of 1919, and the third in the winter of 1920. The nasopharyngeal materials were obtained from those cases of acute uncomplicated influenza which presented a sudden onset with chilliness, fever, prostration, headache, muscular pains, injected conjunctivæ, sore throat and an unproductive cough. Great reliance was placed on leukopenia affecting the absolute number of the mononuclear cells, chiefly of the lymphocytic variety. The unfiltered nasopharyngeal secretions from eight cases of uncomplicated influenza in the first thirty-six hours of the disease, and from twelve cases in the later stages of the infection, were inoculated into the lungs of rabbits. The washings from seven of the eight early cases produced fever, indisposition, listlessness, ruffled hair, conjunctivitis and a marked leukopenia in the rabbits. The symptoms began in from twenty-four to forty-eight hours after inoculation and persisted for about three days, the animal then returning to normal. If the

rabbits were killed, edema, emphysema and hemorrhagic foci were found in the lungs. Similar syndromes were produced by successive passages of lung-tissue suspensions, the aërobic cultures of which were usually sterile. The material from the twelve cases that were either afebrile or convalescing or in the course of a secondary pneumonia produced no symptoms in the rabbits. All the control tests, which consisted of the injection into the lungs of rabbits of a saline solution, suspensions of normal rabbit lungs, normal rabbit serum, foreign protein, ordinary bacteria, including Pfeiffer's bacillus and its toxin as prepared by Parker's method and, finally, the nasopharyngeal secretions from fourteen apparently healthy persons, failed to show the "familiar clinical and pathological action." The same authors (*II, Jour. Exp. Med.*, 1921, xxxiii, 361) obtained negative results when nasopharyngeal secretions from early cases of uncomplicated influenza were inoculated, intratracheally and subconjunctivally into Macacus rhesus monkeys. On further experimentation, it was found that the "active agent," as it existed in the nasopharyngeal secretions in man and in the lung of rabbits injected with human secretions, passed through Berkefeld V and N candles and was capable of producing the same effects in rabbits as the unfiltered material; that the peculiar effect encountered in the inoculated rabbit could be induced in guinea-pigs and the "agent" withstood the action of sterile 50 per cent glycerol for periods up to nine months. The effect on the rabbit lung of pure cultures of types of organism ordinarily encountered in the aërobic cultures of human nasopharyngeal secretions, alone or in combination with the "influenzal agent," was studied (*III, Jour. Exp. Med.*, 1921, xxxiii, 373). It was found that neither B. pfeifferi nor its toxic extract when injected intratracheally into the lungs of rabbits induced changes similar to those described for the "influenzal agent" or produced a pneumonic consolidation or led directly to the death of the animals. From their works in this series the authors concluded that concurrent infections in the experiments described could be regarded as of accidental nature and were not causally related to the typical effects induced in rabbits by a material wholly free from ordinary bacteria and that the "influenzal agent" exerted an effect on the pulmonary tissue which encouraged the invasion of the lung and subsequent multiplication there of ordinary bacteria. They believed that a similarity existed between the conditions under which concurrent infections arose in the inoculated rabbits and those which seemed to favor the occurrence of concurrent infection during epidemic influenza in man. They call attention to the fact that death did not occur in rabbits as a result of the uncomplicated effects of the "influenzal agent" alone, death being seen only in those animals where concurrent infection of the lung by ordinary bacteria was present.

Albumin Reaction in Sputum.—Conclusions as to the value of albumin reaction as a diagnostic aid in tuberculosis have varied with different investigators since the first determination of Biermer in 1885. Burdick and Gauss (*Am. Rev. Tuberc.*, 1921, iv, 889) reported the results obtained in examining the sputum of 200 patients. Equal parts of sputum and 3 per cent acetic acid were mixed and the clear filtrate was tested by using the Esbach albuminometer tube commonly

employed in urinalysis. Albumin was found positive in 95 per cent of the patients with incipient, in 98.4 per cent of those with moderately advanced, and in 92.6 per cent of those with advanced tuberculosis. It was present in 26 unclassified cases of pulmonary tuberculosis and of all the tuberculous individuals examined, 96.3 per cent had a positive test. In 6 patients with chronic bronchitis and 2 with asthma, no albumin was found in the sputum, whereas 1 case of lobar pneumonia showed the presence of albumin. It was found that the quantity of albumin varied in the various cases from day to day. From their own investigations, the authors concluded that the test is of value as a diagnostic aid in pulmonary tuberculosis.

The Incidence of Bovine Infection in Tuberculous Meningitis.—Some investigators have found 15 per cent of tuberculous meningitis cases in man due to bovine strains. That 49 per cent of the cases in children under five years of age and only about 1 per cent in adults are of the bovine type is startling. NOVICK (*Jour. Med. Res.*, 1920, xli, 239) studied 48 strains of tubercle bacilli from the cerebrospinal fluid of as many unselected cases. Three of these were of bovine type. Indirect isolation was accomplished by subcutaneous injection of the guinea-pig, pure cultures being obtained by culture of inguinal lymph nodes on Dorset's plain egg or glycerin egg media. It was found that, while a moist growth on Dorset's medium was usually indicative of the bovine type, confirmation by demonstration of virulence in the rabbit was necessary. To a degree, the production of pigmentation on egg medium suggested a human origin of the tubercle bacilli, but this characteristic depended upon the age of the culture.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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Studies of the Phenomenon of d'Hérelle with Bacillus Dysenteriæ.—WOLLSTEIN (*Jour. Exp. Med.*, 1921, xxxiv, 467) states that the phenomenon of d'Hérelle is the expression of a lytic reaction occurring between a bacterium which is inducing an infection in an animal and a substance elaborated in that organism, probably by the leukocytes and other tissue cells, in response to the stimulus of the metabolic products of the invading bacterium. The important element

of the reaction is that bacteria exposed to the lytic substance acquire the ability to transfer the lytic property to subsequent generations. It has been shown that a lytic fluid for dysentery bacilli can be obtained from the peritoneum of the guinea-pig by intraperitoneal inoculation of live dysentery bacilli, and that the lytic action of such a fluid is not strictly specific, but that it exerts a group action on the dysentery-colon-typhoid group of bacilli. A lytic fluid with similar effects was obtained from a child dying of Flexner dysentery infection, and an anti-colon bacillus lytic fluid from a child who died of intussusception with colon bacillus peritonitis. The action of the lytic fluid on the dysentery bacilli, both in vivo and vitro, is to divide the culture into sensitive and resistant strains, and the latter can be carried to a degree of very marked, if not complete resistance to lysis. Such resistant strains are not lysogenic, nor are they agglutinable. The sensitive strains are lysogenic and agglutinable. Varying degrees of sensitive and resistant bacilli exist in a single culture. The sensitive bacilli gradually lose the lysogenic property which they acquired under special conditions, but the very resistant bacilli never acquire that property. It is conceivable that the resistant strains are responsible for the untoward outcome of disease in human beings. Theoretically the administration of lytic fluid should rid the intestinal tract of most of the infecting bacilli, and only if completely resistant bacilli in large numbers remain unacted on is the outcome of the disease a fatal one.

Hypochlorite Process of Oyster Purification.—Carmelia, (*Public Health Reports*, 1921, xxxvi, 876) reviews the results of experiments on a commercial scale, having for their object the purification of oysters polluted by sewage. The oysters are treated by two changes of chlorinated water covering a total period of from eighteen to twenty-four hours. The chemical practically sterilizes the water in which the oysters are floated and results in such marked bacteriological improvement in the bivalves that they may be regarded as safe for food, unless the initial pollution has been excessive. It is suggested by the writer that oysters, regardless of origin, might safely be treated in this manner.

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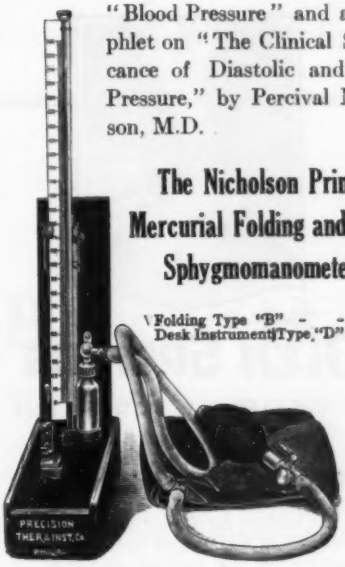

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